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INTRODUCTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (signed to press 8 Feb 83) p 4

[Article by editorial board]

[Text] There has been a considerable increase in requirements pertaining to life support of man in space because of the increased duration of missions aboard manned Salyut orbital stations, diversity of work performed by cosmonauts in crew compartments and during extravehicular activity. In view of these trends in space exploration, questions of assuring radiation safety of spaceflights are acquiring much importance. For example, while the levels of radiation to which the crews of spacecraft of the Soyuz type were exposed (no more than 2 weeks in flight) constituted from several tens to 150-200 mrem, exposure of crews of Salyut stations to radiation reaches 2-3 rem in 6 months, which conforms to the permissible levels of irradiation per year for individuals who work with radiation sources but is appreciably more than the levels set for the rest of the public (NRB [radiation safety standard]--69). With increase in altitude of orbit (which is important to extending the operation of a station), the dose level could increase drastically because of the effects of earth's radiation belts. For example, during the mission of American astronauts aboard the Skylab station in an orbit at an altitude of 433 km, the dosage over the 84-day flight was about 8 rem. An increase in slope of the orbital plane also leads to a greater risk of exposure of cosmonauts to solar cosmic rays. For example, radiation levels may exceed tens of rem during flights over polar orbits.

Under such conditions, it was deemed useful to publish in this issue of our journal a series of articles written by authors who are working on different aspects of the problem of space radiation and its hazard to the body. Publication of these works will help form an idea about the extent of radiation hazard of near-earth orbital missions, the main sources of this hazard, ways and means of minimizing the adverse effects of cosmic radiation on the body, as well as to delineate the basic routes of research on this problem in order to assure the safety of future spaceflights.

SURVEYS

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ELECTROSTATIC SHIELDING AGAINST COSMIC RADIATION (CURRENT STATUS AND PROSPECTS)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 20 May 82) pp 4-7

[Article by T. Ya. Ryabova]

[English abstract from source] Conduction currents of the vacuum atmosphere near the spacecraft were measured in an electrostatic shielding and an electrostatic shielding module in electrostatic fields of about 10^7 Wt/m at a voltage of 3×10^5 V onboard Cosmos-605, 690, 732 and 936. The resultant conduction currents ($\leq10^{-9}$ A/m^2) give evidence that the vacuum environment has high electroinsulation properties which contradicts the concepts derived from ground-based studies. Using up-to-date high-voltage devices, it appears possible to develop an efficient electrostatic shielding which will be of a low weight and a low power consumption.

[Text] The idea of developing effective protection of spacecraft (SC) against the effect of factors of the cosmic environment (meteors, dust particles, diverse contaminants, etc.) by means of magnetic and electric fields is an old one. Thus, already F. A. Tsander advanced the suggestion of creating a magnetic field in an SC in order to retain a cloud of charged dust particles and of protecting the SC against meteors with "static electricity" [1]. Development of these ideas as they apply to active protection of biological objects against charged particles of cosmic radiation began in the 1960's, when it was demonstrated that active protection yields a significantly greater multiplicity of attenuating radiation per unit mass than traditional methods of shielding with use of absorbent materials [2-8]. The relevance of this matter is also due to the fact that, in the case of long-term flights (for example, in geostationary orbit), large-sized radiation shielding is exceptionally effective when there is combined use of fields and absorbent materials [3, 4, 8], and it can be combined well with various SC complexes where use of magnetic and electric fields is required.

Magnetic shielding against radiation (MS) for biological objects is based on creation of "forbidden zones" by means of fields, to which particles of specific energies do not penetrate. It is planned to locate the crew, biological complex and radiosensitive equipment in these zones, to protect them against radiation.

Use of electrostatic fields to deflect incident flux of charged particles from the SC surface served as the basis of electrostatic shielding (ESS). In such

shielding, one can use solid dielectircs or the vaccum surrounding the SC as the electric-insulation medium.

Plasma shielding is based on a combination of ESS and MS principles; in it, the electric field between the charged shell of the spacecraft and electron cloud that is retained near the spacecraft by a weak magnetic field plays a protective role.

The present status of active shielding is such that one can seriously consider only two types, MS and ESS. This is attributable to the fact that the choice of type of active shielding of biological objects, other conditions being equal, is determined primarily by the level of technical and technological development of structural elements of such shielding, as confirmed by full-scale experiments, as well as feasibility of combined use with other spacecraft systems. From this point of view, in spite of the obvious advantage of MS, which provides for concurrent protection against charged particles of different polarity, the degree of readiness of ESS at the present time is unquestionably greater with respect to solving problems of radiation protection (for example, against electrons of earth's natural and artificial radiation belts).

Our objective here was to assess the current status and prospects for development of electrostatic shielding on the basis of the results of experimental studies aboard the biosatellites Cosmos-605, Cosmos-690, Cosmos-782, Cosmos-936 and Cosmos-1129.

The results of studying ESS against protons and electrons were reported previously [2, 3], with consideration of the dynamics of charged particles in electric fields. The methods that were developed to measure radiation levels beyond ESS revealed that working voltage of shielding used for different end purposes (including radiosensitive photographic materials and equipment, crew, biological complex, etc.) is in the range of $(3-7)\cdot 10^7$ V against solar flare protons, $(0.1-5)\cdot 10^5$ V against electrons from earth's natural belts and $(0.8-2.5)\cdot 10^6$ V against electrons from artificial belts. In all instances, the protective electric fields did not exceed 10^7 V/m. However, one can obtain the above-mentioned voltages and fields aboard a spacecraft only when the power consumption of the shielding constitutes a negligible part of the energy resources of the spacecraft. Studies have shown that power consumption is determined mainly by the electric-insulating properties of the vacuum atmosphere surrounding the spacecraft in electric fields of $E \lesssim 10^7$ V/m.

Before the studies of ESS were conducted on biosatellites, all of the conceptions concerning insulating properties of the vaccum environment in the vicinity of a spacecraft in powerful electric fields (because of the absence of any information on this score) were based on the results of ground-based experiments in ESS models and analysis of data on conduction currents of the high-voltage vacuum space mainly of accelerating tubes, which are similar in operating conditions to ESS [3, 9]. With use of these data, which were obtained by different authors, and because of the vagueness of information about the effect of a vacuum environment on its insulating [dielectric] properties, estimates of power consumption of shielding against particles of the opposite sign fluctuated by more than 10^4 times and exceeded significantly the energy resources of modern spacecraft. Moreover, it was assumed that the presence of various gas emissions from the

spacecraft surface in the vacuum space could worsen the properties of vacuum insulation, as compared to laboratory conditions, and create additional difficulties in obtaining high voltage aboard the spacecraft [6, 9, 10].

Thus, obtaining data about the insulating properties of the vacuum atmosphere enveloping a spacecraft, which are determined by conduction currents in electric fields and at voltages required for protection, was of exceptional importance to solving the problem of technical engineering execution of ESS with the present level of high-voltage technology.

Direct measurement of conduction current in the vacuum near a spacecraft at altitudes of 200-400 km in electric fields with $E \leqslant 10^7$ V/m and intensity of $U \leqslant 10^5$ V was first taken on ESS models operating from onboard high-voltage power sources situated on the outer surface of Cosmos-605, Cosmos-690 and Cosmos-782 biosatellites.* The measured low conduction currents $j \leqslant 10^{-9}$ A/m^2 in ESS models that adequately reflected the function of ESS were indicative of high insulating properties of the vacuum surrounding the biosatellite, unlike previous conceptions based on data obtained on the ground [2, 3, 7]. Later on, such conclusions in the case of lower voltage were confirmed by a number of authors for spacecraft used for other purposes [12].

Specific power consumption by ESS with consideration of efficiency of modern high-voltage power sources was determined from the measured conduction currents in ESS models. Maximum specific power consumption did not exceed 1 W/m^2, constituting a negligible share of the spacecraft power resources, at operating voltages in the range of $(0.1\text{-}2.5) \cdot 10^6$ V in the presence of total voltage effect at $U \geqslant 3 \cdot 10^5$ V, i.e., growth of leakage current with increase in voltage at $E = \text{Const} = 10^7$ V/m.

Such low power consumption of shielding, which is essentially due to the high insulating properties of the vacuum near the spacecraft, enables us to check the self-charging hypothesis expounded by K. A. Trukhanov [3] on the basis of the work by V. G. Kurt [13] pertaining to the possibility of creating a shielding negative charge on a surface shielded from ions of magnetospheric plasma and ultraviolet solar radiation, which could be used as a self-contained mode for ESS function. The results of an experiment conducted aboard Cosmos-936 biosatellite confirmed this possibility. Electric fields of $E \sim 10^7$ V/m and volatge of $\sim 10^5$ V were created in the biosatellite by charging the shielded ESS model with a flow of electrons with energy $E \leqslant 10^5$ eV with artificial injection from a high-voltage cathode-ray device situated on the outer surface of the biosatellite. Studies dealing with simulation of self-contained mode of ESS operation without traditional onboard high-voltage power sources not only confirmed the previous findings of high insulating properties of the space environment vacuum, but expanded appreciably conceptions about the possible means of creating high voltage and electric fields in space, in particular for future operation of ESS in a self-contained mode in geostationary orbit, which had been confirmed at lower voltage in [11, 14].

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*It must be noted that at that time there had been no experience in both Soviet and foreign space technology in working with such high-voltage devices aboard spacecraft.

All of the data obtained with ESS models served as the basis for work on finding the means of developing a standard [unified] version of modular ESS in the form of a discrete interchangeable set of standardized element-modules that can completely fill a volume of arbitrary configuration. Studies of insulating properties of the space environment in a composite module with voltage of up to $3 \cdot 10^5$ V were pursued aboard Cosmos-1129 artificial earth satellite. The experimental findings confirmed the results of previously made estimates of power consumption of the shield on the basis of data obtained in ESS models with $U \leqslant 10^5$ V.

As a result of analysis and evaluation of data obtained in models and module of ESS, the basic energy characteristics and mass were defined for ESS of biological objects at the present level of high-voltage technology. The mass of ESS against electrons from natural and artificial radiation belts of earth, in the presence of shelter against protons from solar bursts, is several times lower than equivalent (at same frequency of attenuation) of shielding by a substance. There is a basic possibility of creating shelter based on the ESS principle [2, 6]. This would lower even more the overall mass of ESS.

As for the future of ESS, it is related primarily to investigation of the efficacy of modular ESS capable of offering protection against charged particles of different polarity and expansion of combined use of electric fields aboard spacecraft. With development of methods of estimating the efficacy of such protection on the basis of solving problems of passage of electron and proton radiations through a region with variable-sign heterogeneous electric field in the presence of matter, it is necessary to solve problems of joining and compatibility of electron-proton ESS. Knowledge of the characteristics and parameters of efficacy will make it possible to define the working voltages required for protection against solar burst protons. At the present time, we are faced with the real task of creating a self-contained mode of ESS operation in geostationary orbit in the presence of protection against protons from solar bursts. In the future, instead of shelter as protection against solar burst protons, electric fields could be used.

It must be noted that, at the present time, it is important not only to solve practical problems, but to try to extract from every study in space the utmost benefit at minimal cost. For this reason, it would be desirable, for example, to use the elements of a thin (~ 0.1 kgf/m^2) of the external shield of an ESS with large surface ($\geqslant 10^2$ m^2) as a solar battery.

Thus, experimental studies conducted with model and modular elements of ESS in electric fields of $\leqslant 10^7$ V/m at voltages of up to $3 \cdot 10^5$ V, created near spacecraft, led to a revision of conceptions of the expected difficulties in creating protective electric fields and voltages in space, and demonstrated the feasibility of developing effective antiradiation ESS at the present level of high-voltage technology. Further expansion of combined use of electric fields created for ESS is related to development of accumulators of electric power, high-voltage solar batteries, electric filters to remove microorganisms and mechanical impurities from the spacecraft interior atmosphere, which is a development of the ideas of F. A. Tsander concerning the prospects and possibility of multipurpose use of electric fields created aboard spacecraft.

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POSSIBLE DIRECTIONS OF REFINING CRITERIA OF RADIATION SAFETY OF SPACEFLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 20 May 82) pp 8-14

[Article by Ye. Ye. Kovalev, V. M. Petrov, V. A. Sakovich and M. A. Sychkov]

[English abstract from source] This paper considers the possibility of characterizing space flight radiation safety, using a value which is integrated over the flight time, takes into account the radiation processes in an irradiated body and averages the probability of adverse radiobiological effects with respect to the distribution of solar proton flares of varying intensity. The proposed characteristic is compared with the current standards with reference to a hypothetic interplanetary flight.

[Text] The radiation hazard of spaceflights is manifested by the possibility of reducing the reliability of fulfilling the flight program by the crew and quality of health of crew members. The possibility of undesirable genetic consequences is not taken into consideration because of the limited number of cosmonauts. These conditions are the basis of the "Temporary Standards for Radiation Safety of Spaceflights (VNRB-75)," which have been in effect in our country since 1975 [1]. In view of the fact that during spaceflights one of the sources of ionizing radiation (solar burst protons) is stochastic (both in time of occurrence and fluency of protons), it is necessary to make use of the concept of probability in characterizing the radiation situation and formulating criteria of radiation safety. Thus, in the VNRB-75, not only standard levels of radiation (D_s) were set for projected estimates of protection of manned flying vehicles, but specifications for reliability of protection in the form of probability of not exceeding the standard level of radiation. However, such a criterion of radiation safety formally implies that different times [duration] of exposure to radiation and different proportions of contribution of probable and determined sources of ionizing radiation are equivalent. For this reason, it is deemed desirable to consider the possible means of further refinement of formulation of a criterion of radiation safety of spaceflights as it applies to the task of providing protection against radiation from both determined and probable sources.

The increase in probability of adverse consequences of erroneous action by a cosmonaut as an operator can be considered a rather general characteristic of lowered reliability of fulfilling a flight program by the crew due to worsening of their work capacity related to exposure to radiation. Let $\rho(t)$ be the probability

of error in a solitary action, $I(t)$ frequency of actions and $\Gamma(t)$ significance of error in single action to fulfillment of flight program or probability of adverse consequence to fulfillment of flight program due to error in a single action. Then the probability of such a consequence over entire flight time T will be:

$$R = 1 - \exp\left\{-\int_0^T \Gamma(t)\, I(t)\, \rho(t)\, dt\right\},$$

which, with low value for R, would be:

$$R \approx \int_0^T \Gamma(t)\, I(t)\, \rho(t)\, dt.$$

Accordingly, build-up of R due to radiation, i.e., ΔR, can be considered the characteristic of radiation risk of failure to fulfill flight program, while the condition that this increment would not exceed the permissible value of ΔR_{max} can serve as a general formulation of the criterion of radiation safety of fulfilling flight program. Obviously, ΔR does not reflect a worsening of quality of health after the flight.

Further, we shall proceed from the assumption that $\Gamma(t)$ and $I(t)$ do not depend on probability of error at preceding points in time. Then, only $\Delta\rho(t)$ will depend on the time of radiation exposure $\dot{D}(\tau)$ preceding the considered point in time t. Since $\dot{D}(\tau)$ during spaceflight is determined by chance events, $\Delta\rho(t)$ should include the probability of these events, which presents an independent problem with respect to computation. However, this problem can be simplified if we were to use the concept of effective residual dose, D_{ef} (for example, with the Blair model or some other means), which in turn unambiguously determines at each point in time the increase in probability of error F (D_{ef}). In this case:

$$\Delta\rho(t) = \int_0^\infty F(D_{ef}) \frac{dp}{dD_{ef}} (\dot{D}(\tau), t)\, dD_{ef}$$

The following is an equivalent expression:

$$\Delta\rho(t) = \int_0^\infty \eta(D_{ef}, t) \frac{dF}{dD_{ef}} d D_{ef},$$

where $\eta(D_{ef}) = 1 - \int_0^{D_{ef}} \frac{dp}{dD_{ef}} dD_{ef}$

is the probability of exceeding D_{ef} at a given point in time. Both η and dp/dD_{ef} are the sum of an infinite series of integrals of increasing multiplicity, which corresponds to the number of chance events in the course of the flight [3].

Let us compare the above formulation of the criterion of radiation safety to the criterion contained in VNRB-75. It is not difficult to demonstrate that if there were no recovery processes in the irradiated organism, i.e., $D_{ef} \equiv D$, and if the radiobiological dose-effect function F(D) were stepped in nature, while error in a single action were significant only in the single last action at the

end of the flight, unreliability of radiation protection would be identical to the magnitude of radiation risk.

Assessment of these hypotheses shows that the proposed formulation of the criterion presents no basic difference from the one in current use, and it is indeed more general than the latter. We know that termination of a long-term spaceflight is its most stressful stage since, on the one hand, the effect of various flight factors is felt and, on the other hand, at the end of the mission there are preparations for and performance of landing, for which reason the crew has important operations at this time and cosmonauts are subject to considerable physical and psychological loads. Apparently, the most rigid restrictions should be imposed at this phase on the consequences of exposure to radiation. Of course, in practice, the sequelae of irradiation are important not only at the end of a mission. This is taken into consideration in the VNRB-75, and in a dual way at that. In the first place, at any point in time in flight the probability of not exceeding $D_S(t)$ should not be lower than specified. In the second place, single exposure dose should be limited. In other words, in the VNRB-75, there is implicit consideration of the difference from zero of the product $I(t)\Gamma(t)$ during the entire flight.

Further, we must call attention to the fact that the specified $D_S(t)$ function is such that, if the accumulated dosage equals $D(t) = D_S(t)$, the effective residual dosage calculated with use of the Blair model would be constant and its coefficients would have the following values: irreversible share of damage $\alpha = 0.15$, relative recovery rate $\beta = 0.022$ [4]. Then the residual dosage is 0.33 "Ev".* Thus, the $D_S(t)$ function itself takes into consideration recovery processes. It is only for this reason that it is possible to increase D_S with increase in flight duration. If we were to consider a flight with $D(t) = D_S(t)$, with $I(t)\Gamma(t)$ = const., the general formulation of the criterion of radiation safety leads to $\Delta R \simeq T$, i.e., probability of failure to perform the flight program per unit time will be constant. It is easy to see that there is an analogy to the reliability of technical equipment. In this sense, indication of a constant value, in the VNRB-75, for reliability of protection of a flight of any duration should be considered justified. If the purpose is to plan flights differing in duration with equal reliability of fulfillment of the program as a whole, on the assumption that $I(t)\Gamma(t)$ = const., reliability of protection, as for any system of the craft, should be greater with longer flight duration.

Finally, we come to stepped function F(D) used in the VNRB-75 from the standpoint of general formulation of the criterion. Of course, no radiobiological effect has such a function. But no concrete individual effect is intended in specifying levels of radiation either in space or on the ground. However, there is a logical validation for such a situation under ground-based conditions. When setting permissible levels of ionizing radiation, only determinate sources are taken into consideration. In this case, trying to estimate maximum probability of some adverse radiobiological effect characterized by a certain function F(D) is tantamount to determining the permissible dosage.

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*Translator's note: Ev (Эв in Russian) may be typo for eV (electron volts); however, since the unit Sv (Зв in Russian) also appears in this article and initial Russian letters are similar, quotation marks have been used with Ev to call attention to the ambiguity.

The findings are different when there are probable sources of ionizing radiation, for example, during a spaceflight. In this case, the same reliability of protection, i.e., probability of not exceeding D_S, could be formed with different contribution of determinate sources, i.e., with different real radiation burden on the body. Thus, during the period of minimal solar activity, when the frequency of solar flare protons is lower by a factor of 10 than during the period of maximum activity, protection that meets the reliability requirements according to VNRB-75 actually provides poorer conditions for the crew than protection aboard the spacecraft estimated for the maximum activity period and a flight taking place in this period.

In orbital flights, the question of proportion of contributions to radiation hazard of determinate and probable sources does not arise, since reliability of protection provided by the structure and equipment of the spacecraft is considerably greater than stipulated in the VNRB-75.

The most pressing matter is to refine criteria of radiation safety of spaceflights in the direction of consideration of a smooth dose-effect function. However, since radiobiology has not yet offered recommendations on the use of some F(D) function, but a very definite one, as well as $D_{ef}[D(\tau), t]$ or $\Delta\rho[\dot{D}(\tau), \tau]$ function, estimates were made of the influence of choice of radiation safety criterion on protection of a spacecraft and elements of radiation from different sources.

In the first place, using the criterion that subsequently served as the basis for VNRB-75, a hypothetical interplanetary flight was considered, with use of three variants of engines which determined different times of exposure to radiation: liquid-propellant rocket engine (LRE), low-thrust ion-plasma jet engine that is powered by a nuclear power plant (NPP) and nuclear rocket engine (NRE) [5]. Optimum distribution was selected for distribution of masses of shadow shielding of the reactor and shielding of radiation shelter against solar flare protons and earth's radiation belt in the event of gathering momentum [spin-up?] in the latter with the low-thrust engine. As a result, optimum radiation dosage was obtained for each of the sources for flights lasting up to 1000 days during periods of both maximum and minimum solar activity, as well as the corresponding values for thickness of the radiation shelter shielding. It was found that, in the case of a 1-year flight, the dosage of radiation from determinate sources during the period of maximum solar activity constituted 0.50 "Ev" with the LRE (galactic cosmic rays), 0.75 "Ev" for NRE (galactic rays and NRE), 130 "Ev" for NPP (galactic rays, NPP and protons from earth's radiation belt), and during the period of minimum activity it was 150 "Ev" for all variants, i.e., D_S conformed to the level specified in VNRB-75 for a 1-year flight. This confirms once more the assumption that the radiation load can differ appreciably with equal reliability of protection, which constituted 0.99 in the example we discussed. Moreover, for variants with an NPP, a dosage of 0.70 "Ev" was accumulated in 1-2 months of "spin-up" in earth's radiation belt. During this period, the radiation burden exceeded 0.50 "Ev" which was set in the VNRB-75 for a flight of such duration. However, further exposure led to the same results as in the case of using the LRE (galactic rays).

In the second place, an attempt was made to describe radiation hazard in terms of effective residual dosage. For this purpose, in calculating the probability

of exceeding the given dosage of protons from solar bursts for flights differing in duration, i.e., $\eta(D_s, T)$, analytical approximation of which was used in the above example, we also used the method of statistical trials (Monte Carlo method) to calculate the values of $\eta(D_{ef}, T)$ for $\alpha = 0.15$ and $\beta = 0.022$. Then, in the above-discussed example of an interplanetary flight, we determined accumulation of effective residual dosage from all sources of ionizing radiation and used, as the criterion of radiation safety, the requirement of the same reliability, but in relation to an effective residual dosage of 0.33 "Ev" for flights of any duration. Thus, we provided a sort of consistency with the above example. As a result, we found that the shielding of the radiation shelter must be considerably thicker, i.e., heavier. And this is not by chance. Unlike a monotonously increasing dosage, the effective residual dosage after solar flares, from passing through earth's radiation belt and pulsed operation of the NPP could diminish. For this reason, exceeding $D_{ef} = 0.33$ "Ev" is temporary, and its duration increases with increase in peak value of D_{ef}, which is not reflected in the probability of such an excess. Thus, description of radiation hazard in terms of effective residual dosage makes it necessary to limit it, even for short periods of time and, consequently, thicker shielding is required. Hence, when using the concept of effective residual dosage, the criterion of radiation safety must be integral for flight duration, as in the above general formulation.

In the third place, we effected optimization of radiation protection in the above hypothetical interplanetary flight with a NPP and using as a criterion the probability of certain radiobiological effects characterized by a very definite type of F(D) function. Function 1-F(D) was approximated with the expression $(1-e^{-D/D_0})^m$. On the basis of data in [6], we used the following values for D_0 (in "Ev") and m: 0.80 and 2 with loss of appetite, 0.93 and 3 with nausea, 1.03 and 4 with vomiting, 0.93 and 7 with diarrhea, 1.09 and 100 with erythema, 3.77 and 100 with scaling of skin, 0.38 and 1000 with lethal outcome. It was assumed that there were no recovery processes.

Since the above radiobiological effects differ appreciably in importance to fulfillment of flight program, the probability of their occurrence should be assumed to differ in designing protection.

In order to make possible comparisons to the original version of protection during interplanetary flight, where shadow shielding of the nuclear reactor and radiation shelter are provided, using the method previously described in [7, 8], we calculated the probability of each effect during flights lasting 0.5, 1 and 2 years during a period of maximum solar activity for the shielding that was optimum in the initial variant. For example, for a 1-year flight, we obtained the following figures: 0.37, 0.17, 0.072, 0.016, 10^{-29}, 10^{-72}, 10^{-55}. Then, using the same method, we determined the optimum contributions of different components of radiation and thickness of shielding of radiation shelter that provided the same probability of each of the above-listed radiobiological effects with minimum overall mass of shielding of the radiation shelter and shadow shielding. As a result, with all three of the above-mentioned durations of flights and for all of the effects discussed, the dosage of radiation from the nuclear reactor diminished from 0.19-0.24 Sv [Sievert] to 0.05-0.12 Sv, while mean dosage of solar flare protons increased from 0.04-0.07 Sv to 0.09-0.17 Sv. This corresponds to such a decrease in thickness of shelter shielding and such increase in thickness of shadow shielding that there overall mass was 1-2 tons less than initially.

A reduction of optimum value of dosage of radiation from determinate sources and increase in optimum value of dosage from a probable source are achieved by replacing threshold function F(D) with a smooth one by adding dispersion with reference to threshold value of dosage. Such replacement reflects recognition of the possibility of absence of an effect in the event that, because of powerful proton bursts, the dosage exceeds the threshold value and, at the same time, the possibility of occurrence of an effect with doses from determinate sources, even though they are below the threshold value.

Thus, replacement of the threshold dose-effect function with a smooth one broadens the range of search for the optimum and enables us to obtain variants with less expenditure of mass to assure radiation safety. It should be noted that this conclusion does not depend on accuracy of approximation of the above-mentioned radiobiological effects or consideration of recovery processes. It can be considered that a result was obtained for certain hypothetical effects, which are characterized by such dependence of probability of their occurrence on dosage accumulated in the course of a long-term flight, which was considered in the estimates. What is relevant in this instance is that a conclusion was drawn as to the desirability of considering a smooth F(D) function for effects with a different F(D) function, rather than the extent to which the hypothetical effects correspond to real ones.

We were also impressed by the fact that the reliability of protection stipulated in VNRB-75, which equals 0.01, corresponds in the above-discussed example, to a probability of occurrence at the end of the flight of an effect characterized by D_0 = 1.00 Sv [Sievert] and m = 5-10, which corresponds to a mean dose of 1.60-2.70 Sv.

In the fourth place, we can cite arguments that explain the significance of radiobiological effects characterized by a mean effective residual dose of 0.33 Sv or mean dosage of long-term irradiation of 1.60-2.70 Sv. If we were to imagine a flight with $D(t) = D_s(t)$, i.e., with D_{ef} = const, as well as with smooth function:

$$dF/dD_{ef} = (2\sigma^2\pi)^{-\frac{1}{2}} \exp\{(\overline{D}_{ef} - D_{ef})^2/2\sigma^2\}$$

and take, for the sake of convenience, $D_{ef}/\sqrt{2\pi} = \sigma$, which is close to reality for many radiobiological effects on the organismic level, with $I(t)\Gamma(t)$ = const. we shall have $\Delta R = 0.5/\Gamma T$. For D_{ef} = 0.33 Sv, ΔR = 0.01 and T = 500 days, we find that $I\Gamma = 0.4 \cdot 10^{-4}$ days^{-1}. What could be the sense of such a low value for the $I\Gamma$ product?

Although we do not know what actions have a 50% probability of being erroneous with D_{ef} = 0.33 Sv, if such actions are performed, for example, once a day, their significance to failure to fulfill the flight program in the case under discussion should be considered to equal $\Gamma = 0.4 \cdot 10^{-4}$. Obviously, the same precision and complicated actions performed daily, on the accuracy of which an effective dose of 0.33 Sv could have an influence, cannot lead to failure to accomplish the flight program in the case of an error. Otherwise, one would have to consider the devices that the spacecraft crew handle to be exceptionally unreliable or dangerous. For this reason a value of $\Gamma = 0.4 \cdot 10^{-4}$ refers to a frequency of malfunctions in devices, in the presence of which actions with these devices lead to nonfulfillment of flight program.

There is another possible extreme variant: there are actions the significance of errors in which to failure to fulfill the program equals 1. These are very definitie and distinct actions, the frequency of which is low. However, those actions for which the probability of error is 50% with effective dosage of 0.33 Sv virtually equal zero under normal conditions. For this reason, $I = 0.4 \cdot 10^{-4}$ should be considered the frequency of actions performed in an unusual situation or with abnormal state of the body.

We can examine similarly the intermediate case, when $I \approx 10^{-2}$ and $\Gamma \simeq 10^{-2}$. However, the conclusion will be the same: the criterion of radiation safety contained in VNRB-75 limits the influence of radiation on reliability of performance of the spacecraft crew in an irregular or emergency situation, the probability of which is low. This conclusion suggests, to some extent, the radiobiological effect to which attention must be given in setting function $F(D_{ef})$. Moreover, we see that it is necessary to set a standard for the dependence on effective dose primarily of the $I\Gamma F$ product, since it is necessary to specify a frequency of actions for each effect.

In the fifth place, after determining the order of magnitude of $I\Gamma$, we optimized protection with the criterion in the form of ΔR and with use of the above-mentioned function df/dD_{ef}. We simulated occurrence of solar burst protons by the method of statistical trials (Monte Carlo method), as indicated in [3]. We considered the energy of dosage of galactic cosmic radiation and reactor radiation to be constant during the flight. We calculated the residual effective dosage for each point in time according to the Blair model, with the values we used above, $\alpha = 0.15$ and $\beta = 0.022$ day^{-1}. Integration for flight time was done by summation at 1-day intervals. Protection was optimized by means of successive insertion of values of thickness of shielding of radiation shelter and mass of shadow shielding so that overall mass would remain constant. The obtained values for ΔR, including those corresponding to optimum distribution of mass in both components of shielding, depend on the taken overall mass of shielding and they are proportional to the value of $I\Gamma$. For this reason, only the relative dependence of ΔR on flight conditions is of interest. When flying with an LRE during the period of maximum solar activity ΔR is 1.5 times greater than during the period of minimum activity. With radiation shelter shielding more than 10 g/cm^2 in thickness, when the hazard of protons from solar flares becomes negligible, ΔR remains virtually constant. When flying with NPP but without spin-up in earth's radiation belt, there will be the same difference in the optimum. The optimum is reached with shelter shielding 6-8 g/cm^2 in thickness, and in this range the change in ΔR does not exceed 5%. This thickness is appreciably smaller than in the original variant [5], i.e., we obtained the same result as given above for the case where a smooth F(D) function is considered but the duration of exposure to radiation is not considered. In this case, the positive effect cannot be expressed in units of weight, but if the thickness of shelter shielding were 12-14 g/cm^2, which corresponds to the results in [5], ΔR would be 1.5 times greater.

We also optimized shielding during long-term flight with use of other dose-effect curves characterized by higher values of D_0. We found that the thickness of optimum shielding of the radiation shelter depends little on the type of effect chosen, as was found without considering the time factor of radiation

exposure. This is attributable primarily to the larger dose of galactic cosmic radiation in a long-term interplanetary flight. When flight duration is 300-500 days, it constitutes 1/3 to 1/2 the standard for radiation level. In addition, the result of optimization is determined by the correlation between slopes of curves characterizing attenuation of dosage of each shielding component involved in optimization (radiation shelter and shadow).

In general, it can be maintained that use of a more general formulation of the criterion of radiation safety expands the possibilities for optimization and is not in contradiction to modern criteria in meaning, yielding similar results in comparable cases. The existing computing complications can be resolved with use of a computer. The main difficulty of changing to the general formulation is that the existing radiobiological data have to be translated into a standard function $\Delta\rho[\dot{D}(\tau), t]$.

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DIET FOR HIGH-ALTITUDE MOUNTAIN CLIMBING

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[Article by M. S. Belakovskiy, Ye. B. Gippenreyter and A. S. Ushakov]

[English abstract from source] This paper discusses the experience accumulated in the Soviet Union and other countries concerning the arrangement of meals for mountaineers ascending the highest summits of the world. The discussion is made with reference to the reported data on human physiology at high altitudes. Physiological and biochemical investigations carried out at high altitudes and during experimental oxygen insufficiency indicate changes in the nutritional status and function of digestive organs under these conditions. The paper describes approaches to the optimization of nutrition of mountaineers at high altitudes.

[Text] High-altitude ascents are referable to complex sports that require utmost mobilization of man's physical and mental capacities. To achieve success in such climbs, use of modern scientific knowledge about the physiological and biochemical distinctions of reactions of the human body at high altitudes, as well as practical experience in biomedical support of ascents, plays an important role.

Organization of nutrition under such conditions requires that close attention be given to the specifics of the locality and climate (low partial oxygen pressure, low ambient humidity, drastic temperature changes in the course of the day, high intensity of ultraviolet radiation, extreme brightness of daylight, drastic temperature drop at night, strong winds, etc.). Under such conditions, the diet should be based on both the fundamental bases of the science dealing with nutrition and data referable to high-altitude physiology.

The works of a number of authors are indicative of considerable changes in digestive function and metabolism at high altitudes (and with artificially induced hypoxia). Thus, according to the observations of I. P. Razenkov [1], a prolonged stay at an "altitude" of 4000 m in a pressure chamber elicited a decrease in salivation in essentially healthy subjects. This was associated with increase in the organic part of the solid residue of saliva, urea and lactic acid, amylolytic strength of saliva and spontaneous salivation.

A shortage of oxygen affects primarily the triggering complex-reflex mechanisms of regulation of secretory functions of the digestive system--salivation and the first phase of gastric secretion. Functions that depend on humoral mechanisms of regulation (secretion of pancreatic juice, bile production) are more resistant to this factor, particularly those in whose regulation intramural elements of the autonomic nervous system are involved--pyloric and intestinal secretion. As a rule, under the effect of hypoxic hypoxia there is a decrease in secretion by digestive glands, but the "altitude threshold" is different for different glands. For example, it is 3500-4000 m for salivary glands and 7000-8000 m for intestinal glands [2].

One can observe differences in sensitivity to hypoxia even in the same organ of the digestive system. For example, secretory function of the body and fundus of the stomach is inhibited at an altitude of 4500 m, whereas secretory function of pyloric glands is inhibited only at altitudes over 6000 m. However, with a predominantly carbohydrate diet, changes in secretory activity of gastric glands under such conditions are less marked than on a mixed diet.

In the presence of hypoxia (at altitudes of 6000-8000 m), there is inhibition of bile-production processes in liver cells; one also observes an increase in viscosity of bile and higher levels in it of organic solids, with less marked increase in concentration of bile acids and bilirubin. Secretory activity of the pancreas also changes: decreased secretion of pancreatic juice, lower content of some enzymes, in particular, amylase and trypsin [1, 3-6]. There is inadequate coverage in the literature of the effect of O_2 shortage on motor function of digestive system muscles, particularly on swallowing movements, peristalsis in the esophagus and cardiac part of the stomach. There are only data to the effect that, under such conditions, there is depression of hunger contractions and decrease in motor activity of a full stomach [3]. Experiments on animals and studies with the participation of man revealed slower evacuation of food from the stomach under hypoxic conditions: the more significant the hypoxia, the longer it took to empty the stomach [3]. It is believed that this phenomenon is attributable to a vagopyloric gastric spasm: the oxygen deficiency stimulates the vagus, which leads to contraction of the pyloric sphincter. With further increase in oxygen deficiency, slower evacuation is caused by the direct effect of this factor on stomach muscles. The effect of epinephrine, secretion of which due to activation of the adrenal medulla is intensified in the presence of hypoxia, could be another mechanism.

There is depression of peristalsis of the small and, to a lesser extent, large intestine in the presence of hypoxic hypoxia [3]. However, it must be noted that the stomach and intestine are more resistant to a shortage of oxygen than the central nervous system [7-11], and a moderate decrease in motor function of the gastrointestinal tract under such conditions is of no clinical significance. Nevertheless, the combined effect of hypoxia and substantial dehydration of the body at high altitude has a significant influence on intestinal peristaltic activity and leads to unpleasant signs, such as constipation.

For a long time, it was believed that altitude, even very high (on the order of 7000-8000 m) has little effect on absorption processes in the stomach and intestine [3]. However, special studies and observations made it possible to

detect disturbances in this function. For example, during the many months spent in the "Silver Hut" (laboratory at an altitude of 5800 m in the region of Mt. Everest), the participants in the scientific expedition noticed that the feces became slightly loose, volumonous and "oily" (the latter was particularly marked after intake of fatty food), and this persisted for 2-3 weeks after descending [12]. In the opinion of Milledge [13], this was steatorrhea, a functional disorder of the small intestine leading to impairment of processes of absorption of fats and, perhaps, other nutrients.

The special literature offers information about small (petechial) hemorrhages into the mucosa of the mouth, particularly the inside surface of the lips, at high altitudes [14], as well as occurrence of toothache during "ascents" in a pressure chamber, during high-altitude flights and in the mountains.

According to M. Monge and C. Monge [15] and other authors, intestinal obstruction occurs more often at high altitudes.

In the mountains, one also observes cases of altitude meteorism--distention of the intestine, which develops as a result of excessive accumulation of gas in it due to various causes, including alimentary ones. To avoid this phenomenon, one should limit intake of foods that cause increased gas production (leguminous and others) at high altitudes.

Hemorrhoids are often encountered during mountain expeditions [14, 16, 17]. The elevated intraabdominal pressure due to hyperventilation of the lungs and wearing a heavy backpack are instrumental in their development and exacerbation. Frequent constipation at high altitude is also a predisposing factor for hemorrhoids, since the fecal masses become very firm due to dehydration of the body and it is difficult to pass them through the large intestine.

Diarrhea is not uncommon in the mountains, and it could be due not only to infection, but irritation of the gastric mucosa by minute particles of mica in the potable water of mountain rivers and streams (Nepal) at the approaches to the base camp, as well as intake of undercooked food at high altitudes. A. P. Panin [18] believes that a biphasic change in blood and tissue H^+ concentration is inherent in high altitudes: at first, the pH shifts in the alkaline direction, then the concentration of hydrogen ions changes in the direction of acidity; there is considerable increase in concentration of incompletely oxidized metabolic products (lactic, pyruvic acids, acetone bodies, etc.). A decrease in blood alkaline reserve has been observed, as well as change in oxidation of fatty acids and amino acids, manifested by increased production of acetone bodies and increase in aminonitrogen content of blood. This author believes that a diet with lower protein and fat content, but higher carbohydrate content, optimizes the course of hypoxia at high altitudes.

Highly skilled mountain climbers presented, during an ascent on Mt. Lenin (7134 m), a drastic shift of acid-base equilibrium of blood and appreciable increase in catecholamine excretion in urine [19]. Stock et al. [20] have established that, at high altitudes, there is an increase in human blood free fatty acid and thyroid hormone levels. T. A. Bagdasarova [21] reported stimulation of activity of redox enzymes, including catalase, peroxidase, carbonic anhydrase. There was increase in glutathione concentration.

At high altitudes, human blood presents a decrease in levels of essential and nonessential amino acids (alanine, glutamic and aspartic acids, serine, lysine,

methionine, threonine, tryptophan), as well as increase in concentration of branched amino acids (leucine, isoleucine and valine) [22]. Also noted was inhibition of glutathione peroxidase, glutathione reductase and glucose-6-phosphate dehydrogenase, which leads to accumulation of products of peroxidation--malonic dialdehyde, diene conjugates of nonesterified fatty acids, associated with erythrocyte and mitochondrial lysis. The drop in level of amino acids of the glutamine group and concurrent activation of processes of their transamination and deamination at high altitude are indicative of intensification of gluconeogenetic processes which, in turn, leads us to assume that the body's exogenous glucose requirement increases. On the basis of the distinctions of metabolic conversion of amino acids, authors believe that it is mandatory to increase the carbohydrate allowance in the diet in order to reduce their utilization for gluconeogenesis, which is necessary for active involvement of amino acids in processes of synthesis of structural and functional components of cells. The question of adequate intake of vitamins with antioxidant action, which control peroxidation processes, also merits special attention.

As a rule, basal metabolism is elevated in the mountains. The increase in basal metabolism in subjects who live temporarily at a high altitude is transient, and it is related to additional expenditure of energy for increased pulmonary ventilation, to maintain body temperature, mechanical function of the heart and other functions, intensification of which occurs during the first stage of acclimatization [25].

We know from the experience of mountain climbing expeditions that there is a change in gustatory function and, sometimes, its distortion at high altitudes [3, 8, 11, 34-38]. Some people start to prefer mainly sour, sweet or salt food, while others wish for some special foods that are impossible to obtain; others yet develop an aversion for fatty food or certain traditional foods used on expeditions, such as canned stewed meat, etc.

Many authors have noted a change in gustatory sensations [11, 38, 39]. It was observed, for example, that high-altitude climbers add extra sugar to their tea to obtain the customary flavor because of duller perception of sweet. For the same reason, to enhance stimulation of gustatory receptors (which serves as a triggering mechanism for many unconditioned reflexes that stimulate activity of digestive organs), it is desirable to add flavorful ingredients, in the form of spices and condiments, to food, which improve not only its flavor, but aroma. The latter circumstance plays a rather important part, since gustatory reception is related to olfactory reception, and it is sometimes necessary to stimulate not only gustatory receptors, but olfactory ones, as well as tactile, temperature and other receptors of the oral mucosa for a gustatory sensation to appear. We refer to mustard, pepper, bayleaf, essences, alimentary acids, etc. A decline and sometimes absence of appetite at high altitude is an adverse sign, which is indicative of insufficient acclimatization, development of mountain sickness, altitude-related deterioration or other pathological states. The appetite may be particularly poor (even to the extent of aversion) in the mornings, after waking up. This is attributable, in part, apparently to the fact that the body experiences even greater hypoxia as a result of hypoventilation while asleep at high altitudes and insufficient arterial oxygenation. Thus, Powles et al. [40] found that there were lower levels of arterial blood oxygenation in 20 subjects 20-35 years of age during nocturnal sleep at an altitude of

5350 m (Mt. Logan, Canada), as compared to data recorded during the waking period. With acclimatization, as well as additional oxygen, the appetite usually improves. Aside from hypoxia, low temperature, dehydration, physical fatigue, the psycho-emotional state and other factors can have a strong influence on appetite and nutritional behavior of mountain climbers when ascending to high altitudes.

The initial loss of weight is related chiefly to dehydration and expenditure of fat reserves in the body, and in the case of prolonged and severe hunger, also to the use of other structural elements of the body, including muscle tissue [41].

A stable body weight combined with normal appetite is a sign of good acclimatization and athletic form. However, when the individual limit of tolerance of altitude is exceeded, weight loss occurs even in the case of adequate food and fluid intake. For example, during the long stay in the "Silver Hut" at an altitude of 5800 m in the Himalayas, members of the 1960-1961 scientific expedition presented progressive worsening of appetite and weight loss, in spite of the fact that they forced themselves to take 3000 kcal/day of food. They lost 453-1360 g per week, and by the end of the expedition weight loss ranged from 6.4 to 9.0 kg. A descent for a few days to 4572 m improved their appetite and body weight. The well-acclimated members of the 1953 British expedition to Mt. Everest lost an average of 1815 g in 4 weeks which they spent at an altitude of about 6400 m, whereas the poorly acclimated participants of the 1952 expedition to Cho-Oyyu lost an average of 4989 g [16, 41-43]. Members of the American 1958 expedition to Hidden Peak (8068 m) lost an average of 9 kg each in 2 months [44]. The continuous weight loss, in spite of adequate intake of calories during long stays at high altitudes is indicative of serious deviations of nutritional status. The loss under these conditions is related to impairment of absorption processes, particularly with regard to fats, in the small intestine [13, 16], protein metabolism [45], intermediate metabolism [26] and other causes.

If we were to assess the opinion of most researchers who studied the effects of high altitudes on man, we could arbitrarily divide high altitudes into the following zones, within the limits of which certain changes occur: zone of complete acclimatization, up to 5300-5400 m in altitude, when adequate rest and diet restore expended energy completely. It is possible for man to live permanently up to these altitudes (and indeed there are such residents); zone of incomplete acclimatization, up to an altitude of 6000 m; adaptation zone (6000-7000 m), where the body's compensatory mechanism function under great stress and complete restoration of vital forces is still possible, but is obtained with great difficulty and for a limited period of time; zone of partial, temporary adaptation (7000-8000 m). There, the energy balance becomes negative, since the body is able to only partially replenish expended energy; for this reason, man can remain in this zone at the expense of his endogenous functional and energy reserves until they are exhausted. Stays at such altitudes should be limited in duration and alternate with descents to altitudes at which complete recovery is possible. The example of the 1950 Frensh expedition to Annapurna (8075 m) shows the consequences of failure to adhere to this rule. Its participants were the world's first to conquer a peak in excess of 8000 m, but they paid dearly for this accomplishment. In their haste to reach their goal before the monsoon season, the mountaineers faced a storm without having regained their strength at lower altitudes, without the necessary reserve of energy. The descent from that peak, which had tragic consequences, was a

graphic illustration of how the depleted body is unable to struggle with hypoxia and starvation, as well as the cold. The zone above 8000 m is called lethal: "survival" is the only suitable term to describe the state and behavior of man at such altitudes, where a mountaineer spends 3-4 days almost exclusively at the expense of his internal resources [8, 10, 13, 36, 41, 42, 46-49].

It is very difficult to determine with sufficient accuracy the energy requirements of a mountain climber during ascents to peaks. This circumstance apparently explains, at least in part, why rather contradictory figures are cited in the special literature on this score.

It has been shown that the energy expended by a man of average height, weighing 65-70 kg, when climbing a mountain constitutes 3.3 to 16.0 kcal/min or 200 to 960 kcal/h [50]. Consequently, on a hike lasting 8 h, the daily expenditure (counting the energy required for basal metabolism and digestive processes) should be 5500-6000 kcal. When climbing to peaks at an altitude of 5000-7000 m, however, and during lengthy traverses at high altitudes, when mountaineers are in motion for 12-14 h/day, energy expenditure is even greater. In high altitude mountain regions, the average daily energy expenditure for moderately heavy work is 4600 kcal. During a march in the Caucasus in the summertime, at an altitude of 2500-3000 m, the energy expended by a soldier constituted 58.2-62.8 kcal/kg body weight, which constitutes 3841-4144 kcal/day when scaled to an average weight of 70 kg. Energy expenditure of border-guards, on duty at altitudes of 4000-4500 m above sea level, with relative light physical work load in the summertime, constituted about 3497 kcal. At an altitude of 2200 m, the same individuals expended more energy, 4019 kcal/day, since they had to do much walking because of the topography of the locality [51].

We know from the practice of ascents that mountain climbers carry up to 25-30 kg packs. Energy expenditure under such conditions constitutes 600-800 kcal/h during ascents and 300-400 kcal/h during descents.

In the book, "Recommendations for Athletes' Diet" [52], the basic types of sports were arbitrarily divided into five groups in accordance with energy expenditure, in order to offer a tentative idea about average energy expenditures. Mountain climbing was classifed in the fourth group, which involves prolonged physical loads, where mean energy expenditure is 5500-6500 kcal/day. V. N. Morozov [35] cites data on his recommended food allowance for mountaineers on the basis of the estimate that caloric value is 6020 kcal at altitudes of 4000-5000 m and drops to 4000-5000 kcal at 6000-7000 m. According to Ward's estimate [41], energy expended during ordinary ascents in the Alps lasting 10 h constitutes about 6000-7000 kcal/day at altitudes on the order of 3000-4800 m.

As for ascents in the Himalayas and the Karakoram range, the caloric value of food taken by participants of such expeditions fluctuated over a rather broad range. For example, in the early expeditions on Everest, caloric value of food did not exceed 2000 kcal/day at altitudes on the order of 5200-6400 m, and it dropped to 1500 kcal/day at higher altitudes (over 7300 m) [36]. As a result of inadequate food intake, there was severe weight loss, not only due to utilization of fat reservoirs and fluid loss, but due to depletion of muscle mass. One of the participants of the 1933 Everet expedition lost so much weight after a long stay at high altitudes, in the course of which he climbed

to 8743 m without using additional oxygen, that he could encircle his thigh with the fingers of one hand [41].

Subsequently, the provisions for food energy for Himalayan expeditions were increased. For example, during the 1952 Swiss expedition on Mt. Everest, daily food intake constituted 3500 kcal [53]. During the English expedition in the same year on Cho-Oyyu, average caloric value of food during approaches to the peak constituted 4200 kcal and at altitudes of 5800-6700 it was 3200 kcal [36]. During the first attempt of Indian mountaineers to climb up Mt. Everest in 1960, caloric value of food was about 5500 kcal up to an altitude of 5500 m, and it dropped to 3000 kcal/day when climbing to higher altitudes [53]. During one of the climbing expeditions of Czech mountaineers, the camp food allowance at an altitude of 4000 m above sea level constituted about 4500-4600 kcal, while the diet intended for 5000-6000 m consisted of 4000-4300 kcal; the assault diet at altitudes of over 7000 m constituted an average of 2200-2400 kcal/day/person [55]. During the expedition of American mountaineers on Mt. Everest in 1963, the assault food allowance had a very high caloric value--5270 kcal per person [56].

G. Huber, in the book "Mountaineering Today" [57], voices the opinion that the food intake could constitute 2000 to 5000 kcal/day, depending on the loads. In a Soviet textbook on mountaineering [34], it is stated that the food intake at a base camp should constitute 5500-6000 kcal/day. These figures do not jibe with the calorie requirements cited in some other sources, according to which a mountain climber requires about 4200 kcal up to an altitude of 5000 m and no more than 1500 kcal/day at altitudes of 5000-6000 m [58]. It is to be assumped that it is hardly desirable to lower the calories this much. At the same time, it should be borne in mind that the body cannot take and assimilate a large volume of high-calorie food at maximum altitudes, because of decrease and sometimes even absence of appetite, practical difficulties in preparing hot food and impairment of processes of utilizing nutrients. For this reason, one must be prepared for deliberately taking in somewhat fewer food calories when assaulting a peak and rely on the body's inner reserves.

It must be noted that, because of the metabolic distinctions at high altitudes, there is a substantial change in requirements referable to different nutrients. Under such conditions, most authors suggest that the share of carbohydrates be increased and fats be limited. Thus, Mitchell and Edman [59], who analyzed the literature dealing with the effect of a high-carbohydrate diet, demonstrated its efficacy in the presence of diverse types of hypoxia. They stressed the fact that such diets attenuate the severity of clinical symptoms of mountain sickness, increase work capacity and efficiency of mental activity.

Subsequently, Astrand [60] and Consolazio et al. [61], who made a study of the symptoms of mountain sickness, demonstrated that carbohydrate diets have a beneficial effect on the organism after rapid ascents to high altitudes and that they improve work capacity. These authors established that maximum work time referable to large physical loads was 3 times longer with use of a high carbohydrate diet than high protein (low carbohydrate diet) diet. Intake of a liquid diet containing a considerable percentage of carbohydrates (68%) and a small share of fat (20% of daily caloric intake) for 12 days at an altitude of 4300 m led to appreciable attenuation of the subjects' symptoms of mountain sickness, in contrast to those who were on the normal liquid diet (control). The

subjects in the experimental group felt better, were more energetic and cheerful. Van Lier and Stickney [3], A. F. Panin [18], G. R. Rung [62], N. N. Sirotinin [63], A. A. Aldashev et al. [64], Pugh [43], Ward [41] and many others have also cited information to the effect that a diet with high carbohydrate content is a means of preventing mountain sickness, alleviates its severity and increases work capacity in the presence of hypoxia. Several authors have indicated that sugar not only attenuates the inhibitory effect of hypoxia, but appreciably retards development of the profound signs it induces [1, 65]. Prolonged and intense muscular work leads to great expenditures that could deplete the body's carbohydrate reserves. Hence there is a need to replace these reserves by intake of carbohydrates during the trip. Ordinary sugar and glucose (grape sugar), which are rapidly absorbed, are indicated [12, 35, 52, 61, 63, 66, 67 and others].

It is best to take small quantities of sugar in the course of the entire day. Such a schedule always eliminates the feeling of hunger and postpones for 1-1.5 h onset of fatigue. For high-altitude climbers, fructose is of particular interest, and it is present in large concentration (40%) in honey. As shown by Reinafarje et al. [67], this monosaccharide is a more efficient energy substrate at high altitudes than at sea level.

There are different opinions concerning fat intake in the mountains. Most authors tend to believe that, while man willingly consumes fatty food in polar regions, he does not have such a desire at high altitudes and a diet with high fat content causes mountaineers to feel worse. The experience of Soviet mountaineers has shown [35] that fats in any form are consumed very unwillingly at altitudes above 4000 m, and that they cause aversion, nausea and, occasionally, vomiting. Many mountaineers do not eat fats at all at high altitudes. At the same time, one should apparently not reduce drastically the amount of fat in the diet at high altitudes where hypoxia is associated with cold temperatures, since it is of high energy value and the main exogenous source of fat-soluble vitamins [68, 69]. In this regard, it is desirable to use complete lipids (vegetable oil and butter), which are better assimilated at high altitudes than solid animal fats.

Of special interest are studies of the influence of the protein in the diet on vital functions in the mountains, since it is a known fact that the body's endurance of extreme factors is worse when there is a shortage of protein or it is biologically unsatisfactory [1]. In the opinion of V. N. Morozov [35], protein should constitute 12% of the daily food calories for mountaineers who are active at a high altitude. Intake of large amounts of protein is hardly desirable, because its oxidation is diminished in the presence of hypoxia. G. Ye. Vladimirov et al. [24, 65], who studied parameters of nitrogen metabolism in the mountains (4250-5300 m above sea level), concluded that a protein load (300 g) leads to considerable increase in nitrogen excretion. In the opinion of the authors, this indicates diminished assimilation of proteins. On this basis, it can be concluded that the standards for protein content in the diet used for lowlands would also be satisfactory at high altitudes, and that it would be desirable to increase the carbohydrates in the food allowance to take care of energy expenditure and increased heat production.

There are rather diversified recommendations pertaining to the proportion of protein, fat and carbohydrates in mountain diets. For example, in the

Himalayan expedition of mountaineers from CSSR, the percentile proportion of protein (fats) and carbohydrates at the base camp, at an altitude of 4000 m, was 14:22:64; it was 10:20:70 at 5000-6000 m and 7:18:75 in the assault diet at over 7000 m altitude [55]. In the opinion of V. N. Morozov [35], the proportion should be 12:23:65 at up to 4000 m and 10-12:22-24:68-70 at 4000-7000 m. Tillman, a participant in prewar expeditions on Mount Everest [70], gives a different proportion--30:10:60, while the Soviet physician-mountaineer, G. R. Rung [62] writes that, unlike previous recommendations for rations for mountain ascents (1:2:10), the proportion of protein, fat and carbohydrate was 1:1:2 during the expeditions of mountaineers from Chelyabinsk on Tyan Shan and the Pamyrs.

It has been established that the efficacy of acclimatization processes and man's work capacity depend, to some extent, on vitamin supply of the body [71-73]. Vitamins are more effective when used in complexes [74-77]. However, this does not rule out the desirability of taking separate vitamins (primarily those with antioxidant action) for specific effect on regulation of some metabolic process or other [78-81].

In the high-altitude environment, there is substantial increase in emission of moisture by the body, mainly through the lungs, when breathing with virtually dry air. This should be compensated by increased fluid intake in order to prevent onset of fluid deficiency and development of dehydration of the body, since dehydration has an adverse effect on well-being, morale and work capacity of mountaineers. Water intake at high altitudes should constitute up to 4 ℓ/day.

When there is profuse perspiration, it is obviously important to replace the loss not only of fluid but minerals. Moreover, since the water recovered from snow and ice contains virtually no salts, it is probably desirable to specially mineralize drinking water during long-term (many months) stays in a high altitude zone [82].

One should include acid foods in the diet for mountain expeditions. This is attributable to development of respiratory alkalosis with hyperventilation at high altitudes and formation, during acclimatization, in body tissues of organic acids which, as they pass into blood, lower its alkaline reserve. Addition of acid ingredients to food and fluids depresses alkalosis, partially prevents mountain sickness and raises the "altitude ceiling" [18, 19, 62, 63, 66, 83].

Thus, studies and experience in organizing high-altitude ascents are indicative of substantial functional changes in the body, depending on the altitude and conditions under which the expeditions occur. These changes are markedly adaptive in nature. Adequate nutrition is of practical importance and could play a deciding role during ascents.

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EFFECT OF 140-DAY FLIGHT ON BLOOD AMINO ACID LEVELS IN COSMONAUTS

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[Article by I. G. Popov and A. A. Latskevich]

[English abstract from source] The results of studying 17 free amino acids in the plasma of the 140-day Salyut-6 crewmembers are presented. The measurements were carried out by means of a Hitachi KLA-3B amino acid analyzer. The data obtained give evidence that the dietary uptake of amino acids before and during flight should be better controlled, the dietary content of amino acids should be enriched with certain amino acids (primarily methionine and cystine) and more adequately balanced. It is recommended to select space diets on an individual basis, taking into consideration anthropometric and metabolic characteristics of cosmonauts.

[Text] With increase in duration of missions, we can expect more profound and persistent metabolic changes in cosmonauts. They can occur both under the effect of adaptive changes in the body and as a result of constant exposure to the set of unique factors of their habitat and prolonged neuropsychological tension. Against the background of change in correlation between anabolic and catabolic processes during exposure to weightlessness and hypokinesia, decreased expenditure of energy, as compared to preflight conditions, we can expect biochemical changes in protein metabolism. Unusual inflight diet could also have some effect. For this reason, it is of interest to study the dynamics of free amino acid levels in blood plasma before and after flights in order to assess amino acid and protein metabolism during spaceflights, adequacy of diet, functional state of the liver, kidneys and other physiological systems of the body, as well as to work out measures to improve the diet of flight vehicle crews and prevent the adverse changes in health status of cosmonauts [1-4].

We submit here the results of a study of blood free amino acid levels in the commander (CDR) and flight engineer (FLE) of the Salyut-6 orbital station before and after their 140-day mission.

Methods

Levels of 17 free amino acids in blood plasma of cosmonauts were assayed in samples of venous blood, which was taken on a fasting stomach before the flight in the course of preflight clinical and physiological examination and

on the 1st day after completion of a 140-day flight. In blood samples that were taken and processed by the standard methods, amino acids were assayed using a model KLA-3B Hitachi automatic amino acid analyzer, which operates on the principle of ion-exchange chromatography [4, 5-9]. Dynamic analysis was performed of the found concentrations of amino acids, and they were compared to findings of other authors [10-12] obtained in relation to other types of work, diet and vital functions, as well as to the results of examinations of the cosmonauts [2-4].

Results and Discussion

Table 1 lists the concentrations of free amino acids in blood plasma of the CDR and FLE before and after their 140-day flight. According to the data it contains, before the flight, the plasma levels of most amino acids in both cosmonauts were in the range of "tentative data" for adults cited by I. S. Balakhovskiy in the third edition of the Great Medical Encyclopedia [10].

Table 1. Levels of free amino acids (mg%) in blood plasma of crew of the Salyut-6 scientific orbital station before and after 140-day flight

AMINO ACIDS	CDR			FLE			DATA OF OTHER AUTHORS			
	PRE-FLIGHT	1ST POST FLIGHT DAY	INFLIGHT CHANGE	PRE-FLIGHT	1ST POST-FLIGHT DAY	INFLIGHT CHANGE	I. B. ZBARSKIY (MEANS)	I. S. BALAKHOVSKIY (TENTATIVE DATA)	MULLER: MEAN DATA	MULLER: RANGE OF FLUCTUATIONS
ESSENTIAL:										
LYSINE	2,57	1,86	—0,71	2,29	1,91	—0,38	2,72	1,0—4,0	2,54	2,11—3,09
THREONINE	1,93	2,56	+0,63	4,14	3,48	—0,66	1,67	1,0—3,0	1,94	1,22—2,93
VALINE	1,86	2,10	+0,24	2,74	2,18	—0,56	2,88	1,5—3,0	1,99	1,36—2,66
METHIONINE	0,19	0,27	+0,08	0,37	0,31	—0,06	0,52	0,3—0,7	0,32	0,23—0,39
LEUCINE	1,30	0,74	—0,56	1,77	1,26	—0,51	1,86	1,0—3,0	1,32	0,93—1,78
ISOLEUCINE	0,68	0,36	—0,32	0,81	0,65	—0,16	1,34	0,5—1,0	0,71	0,46—1,15
PHENYLALANINE	0,84	0,44	—0,40	1,00	0,69	—0,31	—	0,5—2,0	0,95	0,63—1,92
NONESSENTIAL:										
CYSTINE	0,63	0,46	—0,17	0,53	0,68	+0,15	1,47*	1,0—3,0	1,77	1,15—3,37
TYROSINE	0,65	0,48	—0,17	1,03	0,68	—0,35	1,04	0,6—2,0	0,91	0,65—1,14
ALANINE	1,75	1,92	+0,17	2,20	1,42	—0,78	3,40	2,0—4,0	3,07	2,22—4,47
ARGININE	0,97	0,72	—0,25	1,85	1,02	—0,83	1,62	1,0—3,0	1,43	0,86—2,63
ASPARTIC ACID	0,22	0,04	—0,18	0,19	0,06	—0,13	0,03	2,0—5,0	0,22	следы — 0,72
HISTIDINE	0,72	0,76	+0,04	0,60	1,07	+0,47	1,38	0,8—2,0	1,24	0,97—1,45
GLYCINE	1,58	1,00	—0,58	1,47	1,35	—0,12	1,50	1,0—4,0	1,74	1,08—3,66
GLUTAMIC ACID	2,92	0,86	—2,06	2,61	1,21	—1,40	0,70	0,7—4,0	0,86	0,25—1,73
PROLINE	1,87	0,97	—0,90	2,78	1,93	—0,85	2,36	0,5—3,0	2,71	1,28—5,14
SERINE	1,11	0,67	—0,44	1,33	1,50	+0,17	1,12	1,0—2,0	1,18	0,68—2,03

*Cystine (+ cysteine).

Methionine, cystine, arginine, aspartic acid and histidine were an exception for the CDR, while threonine, cystine, aspartic acid and histidine were an exception for the FLE, and their levels differed from the standards cited in the BME [Great Medical Encyclopedia](see Table 1).

Cystine content in plasma was below the "tentative data" [10] in both cosmonauts (0.37 mg% less for the CDR and 0.47 mg% less for the FLE). We discussed in detail the possible dietary and individual causes of this phenomenon in our previous reports [4]. It should be noted, however, that the crew members of the Salyut-5 orbital station, who were generally on an analogous preflight diet when preparing for missions, presented a lower concentration of cystine than the bottom of the range of "tentative data." Thus, in the crew of the first expedition aboard Salyut-5, preflight concentration of cystine constituted about 0.73 mg% in the CDR and 0.57 mg% in the FLE [4]; in the crew of the second expedition, the figures were 0.71 and 0.74 mg%, respectively. A. S. Ushakov and T. F. Vlasova, who examined some cosmonauts, found similar cystine concentrations, 0.73±0.004 [2, 3].

Consequently, the concentration of cystine was rather similar in the crews of Salyut-6 and Salyut-5, as well as other cosmonauts [2, 3] before flights. The method (ion exchange) of assaying amino acids and time of taking blood samples were identical. For this reason, the demonstrated preflight level of plasma cystine was most likely attributable to the same causes in the cosmonauts: similar diets, similar living conditions, similar physical and neuropsychological loads during flight training, high clinical and physiological parameters of health status, little difference in ages. A comparison of these figures to the findings of certain other authors [for example, 11 and 12], revealed that the cystine concentration was somewhat lower in the preflight period in the crews of Salyut-6 and Salyut-5 than cited as the "standard" by these researchers (see Table 1). Why was the concentration of cystine somewhat lower in all tested cosmonauts than cited in the "tentative data" for adults [10]? This question requires further investigation.

The concentration of aspartic acid in both crew members of Salyut-6 was very similar preflight and also appreciably lower (by 1.78 mg% in the CDR and by 1.81 mg% in the FLE) than the bottom range of "tentative data" for adults [10]. If we compare the values for aspartic acid to the figures of other authoritative sources (for example the data cited by G. Muller [12] or I. B. Zbarskiy [11]), the findings would be somewhat different (see Table 1). It should be noted, first of all, that in both cited works, generally lower concentrations of aspartic acid are reported than in the "tentative data" of I. S. Balakhovskiy [10]. According to the data of G. Muller [12], the concentration of aspartic acid in plasma of both cosmonauts before the flight was not only in the range of the "physiological norm," but even virtually on the level of its mean, which is 0.22 mg%, particularly in the CDR. The mean aspartic acid level cited by I. B. Zbarskiy in blood plasma of adults was even lower than the preflight parameters for the crew of Salyut-6 and substantially lower than the "tentative data" [10]. Thus, according to these sources [11, 12], plasma aspartic acid content was in the normal range for the CDR and FLE of Salyut-6, and it was not low. Examination of the Salyut-5 crew before flight revealed that plasma aspartic acid content was also substantially lower than the "tentative data" in BME [10] and rather close to the figures established for the Salyut-6 crew. Thus, preflight concentration of aspartic acid in plasma in the crew of the first expedition in Salyut-5 was as follows: 0.11 for the CDR and 0.32 mg% for the FLE [4]; the figures for the crew of the second expedition were 0.14 and 0.21 mg%, respectively. According to the data of G. Muller [12], these figures are in the "normal" range, but according to I. B. Zbarskiy they are substantially higher than the mean

"physiological norm" (see Table 1). All this warrants the belief that the Salyut-6 crew had a normal aspartic acid content in plasma for their occupational group. This is also confirmed by the data of A. S. Ushakov and T. F. Vlasova [2, 3], who demonstrated an even lower level of aspartic acid (0.11±0.01 mg%) in the 30 cosmonauts they examined.

Preflight histidine content of plasma was somewhat lower in both cosmonauts than the bottom range for adults, according to some authors [10, 12] and substantially lower than the mean "physiological norm" cited by I. B. Zbarskiy in BME (3d edition) [11]. It should be noted that the figure cited by I. B. Zbarskiy, as compared to the tentative data of other authors [10, 12], does not appear to be the mean, but closer to the top of the "normal" range (see Table 1). Analysis of blood plasma of the crew of Salyut-5 orbital station before flight revealed higher concentrations of histidine. The level of this amino acid constituted 0.89 mg% for the CDR and 1.29 mg% for the FLE in the first Salyut-5 expedition [4], 1.68 and 1.31 mg%, respectively, for the crew of the second expedition.

Thus, the preflight concentration of histidine in the crew of Salyut-5 was closer to the mean figures cited by I. B. Zbarskiy [11], G. Muller [12] and I. S. Balakhovskiy [10] than the concentration of this amino acid in the crew of Salyut-6. A. S. Ushakov and T. F. Vlasov cite closer figures, but still they are higher, 0.88±0.06 mg%, than our analysis of histidine concentration. All this compels us to consider the plasma histidine content to be somewhat low in the CDR and particularly FLE of Salyut-6. The causes of this finding are still not entirely clear.

Preflight methionine content of plasma was 0.11 mg% less in the CDR than the bottom of the range of "tentative data" of I. S. Balakhovskiy [10], 0.04 mg% less than the "norm" of G. Muller [12] and substantially lower than the mean figures cited in [11, 12] (see Table 1). The low plasma methionine concentration in the CDR could have been due to the dietary factor. The CDR presented a low concentration of cystine, below the "normal" levels cited by other authors. For this reason, when there is a shortage of cystine in the diet, the methionine in food and from endogenous sources could be partially utilized for its synthesis, which could lead to decrease in plasma cystine concentration. In the FLE, the preflight concentration of methionine in plasma was in the "normal" range [10-12], but somewhat above the mean figures cited by G. Muller [12] and below those of I. B. Zbarskiy [11]. According to the "tentative data," the concentration of methionine in the FLE was close to the bottom of the "normal" range. The demonstrated differrences in plasma methionine content in the CDR and FLE could be attributable to some differences in their actual individual diet (for example, different intake of meat, eggs, cottage cheese of the amounts in the issued food allowance or additional intake of food containing methionine). The preflight concentration of methionine was in the range of the "tentative data" in both crews of Salyut-5, but also different appreciably in different individuals. A. S. Ushakov and T. F. Vlasova cite figures that are close to ours: 0.26±0.01 mg% [2, 3].

We were impressed by the relatively high concentration of plasma threonine in the FLE prior to his flight. While in the CDR the threonine content was in the range of normal and even mean levels indicated by the above-mentioned authors, in the FLE this parameter was substantially higher. The FLE had

1.14-1.21 mg% more threonine than the "standards" [10, 12] and 2.47 mg% more than the mean "norm" of I. B. Zbarskiy [11]. If we were to continue making comparisons with the results of testing Salyut-5 crew members that were published earlier [4], we would conclude that none presented as high a concentration of threonine as the Salyut-6 FLE. Plasma of the CDR of the first Salyut-5 expedition contained 2.13 mg% threonine and that of the FLE 2.99 mg%; the figures for the crew of the second expedition were 1.6 and 1.98 mg%, respectively. A. S. Ushakov and T. F. Vlasova also cite lower figures: 2.56±0.13 mg%. Consequently, preflight plasma threonine content for the crews of Salyut-5 was in the range of "normal values" published by other authors, although it was somewhat higher than the mean "physiological norm" in the crew of the first expedition [10, 12]. Individual dietary differences, in particular, unbalanced amino acid content of food, could be the cause of such a high concentration of threonine. The metabolic individuality of the FLE, as compared to other tested cosmonauts, could have played some part. However, the alimentary factor seems to be a more probable cause, since there was a substantial decline of threonine level in plasma after intake of a different diet during the 140-day flight, and it came close to the top range of "tentative data."

Let us compare the preflight "amino acid status" of our two cosmonauts.

The preflight levels of most essential amino acids were higher in the FLE than the CDR. Only the lysine concentration was somewhat higher in the CDR. In the FLE, threonine, valine, methionine, leucine, isoleucine and phenylalanine levels exceeded average normal values according to G. Muller, while lysine content was somewhat lower than "normal." In the CDR, only lysine and threonine content corresponded to or exceeded the indicated mean levels [12], while the concentrations of the rest of the amino acids were lower. As compared to the mean figures of I. B. Zbarskiy, plasma threonine was the only one to exceed the "norm" in the FLE, while the concentrations of the other amino acids were below it. In the CDR, only threonine exceeded somewhat the average "norm" also. It is therefore not surprising that the preflight sum of essential amino acids was higher in the FLE than the CDR (by 3.75 mg%; Table 2). As for the nonessential amino acids, five of them (tyrosine, alanine, arginine, proline and serine) were present in higher concentrations in the plasma of the FLE than the CDR, while the other five, on the contrary, were present in lower amounts. In general, however, the overall amount of nonessential amino acids was still larger in the FLE than CDR (by 2.17 mg%). As compared to the means cited by G. Muller, four (tyrosine, arginine, glutamic acid and proline) were present in FLE in a "normal" or above normal concentration. The concentration of the other six nonessential amino acids was below the normal mean. In the CDR, only two nonessential amino acids (aspartic and glutamic acids) corresponded to the average normal levels in plasma [12]. If we compare the data in Table 1 to the means cited by I. B. Zbarskiy, six nonessential amino acids (tyrosine, arginine, aspartic and glutamic acids, proline and serine) conformed to the "norm" or exceeded it in the FLE, while the other four were present in lower concentrations. In the CDR, the concentration of only four amino acids (aspartic and glutamic acids, glycine, serine) corresponded to the mean levels or exceeded them [11]; the rest of the plasma amino acids presented lower levels.

Thus, the impression is gained that the preflight levels of essential and, to a somewhat lesser extent, nonessential amino acids were higher in plasma of the

FLE than the CDR. Indeed, the total sum of preflight amino acids was 5.92 mg% greater for the FLE than the CDR (see Table 2). This could have been due to differences in actual food intake, in spite of the officially identical food allowance served in the mess hall. Both there and at home, the FLE had the opportunity to take in more food, particularly of animal origin. This is indicated by the higher concentrations of essential amino acids in blood plasma of the FLE.

Table 2. Overall levels of 17 free amino acids in blood plasma of crew in Salyut-6 orbital research station before and after 140-day flight (mg%)

PARAMETERS OF AMINO ACID METABOLISM	CDR			FLE		
	PRE-FLIGHT	1ST POST-FLIGHT DAY	IN-FLIGHT CHANGE	PRE-FLIGHT	1ST POST-FLIGHT DAY	IN-FLIGHT CHANGE
TOTAL ESSENTIAL AMINO ACIDS	9,37	8,33	—1,04	13,12	10,48	—2,64
TOTAL NONESSENTIAL AMINO ACIDS	12,42	7,88	—4,54	14,59	10,91	—3,68
OVERALL AMINO ACIDS	21,79	16,21	—5,58	27,71	21,39	—6,32
RATIO OF ESSENTIAL TO NONESSENTIAL AMINO ACIDS	0,75	1,06	+0,31	0,90	0,96	+0,06

On the whole, the "amino acid status" of the FLE was quite satisfactory. The concentrations of cystine, alanine, histidine and threonine were exceptions. In the CDR, this parameter was lower, particularly for methionine, cystine, tyrosine, alanine, arginine, histidine and proline. All this is indicative of the need for stricter and more systematic monitoring of actual food intake and nutritional status of cosmonauts during training for long-term flights and, when indicated, of improving the amino acid aspect of the food allowance.

Immediately after the flight, the CDR presented a decline in blood plasma levels of 12 amino acids (lysine, leucine, isoleucine, phenylalanine, cystine, tyrosine, arginine, aspartic and glutamic acids, glycine, proline and serine) and rise of 3 others (threonine, valine and alanine), while methionine and histidine showed virtually no change, as compared to preflight levels. The FLE presented a decrease in concentration of 13 amino acids (lysine, threonine, valine, leucine, isoleucine, phenylalanine, tyrosine, alanine, arginine, aspartic and glutamic acids, glycine and proline), increase in three amino acids (cystine, histidine, serine), while methionine content underwent virtually no change. Thus, the postflight levels of most amino acids dropped in both cosmonauts. These results conform, to some extent, with those obtained in studies conducted during flights lasting 30 and 63 days [2, 3].

The same direction of changes, a decline, was demonstrated in both cosmonauts with regard to 10 amino acids (lysine, leucine, isoleucine, phenylalanine, tyrosine, arginine, aspartic and glutamic acids, glycine, proline), while a rise occurred in only one amino acid, histidine. Changes in concentration of six amino acids were in different directions. The concentration of threonine, valine, methionine and alanine increased for the CDR and decreased for the FLE;

on the other hand, plasma cystine and serine concentration decreased in the CDR and, on the contrary, increased in the FLE.

After the 140-day flight, the blood plasma levels of 11 out of the 17 amino acids (methionine, leucine, isoleucine, phenylalanine, cystine, tyrosine, alanine, arginine, aspartic acid, histidine, serine), i.e., most of the amino acids assayed, were below the "tentative data" for adults [11] for the CDR. For the FLE, only the concentration of three amino acids (aspartic acid, alanine and cystine) was below the indicated "norm," while the concentration of threonine remained above the "tentative data." In the preflight assays on the CDR, the concentration of five amino acids (methionine, cystine, arginine, aspartic acid and histidine) was below the "tentative data." Consequently, after the 140-day flight, the same five amino acids as before the flight remained below the "tentative data" and, in addition, the concentration of six more amino acids (leucine, isoleucine, phenylalanine, tyrosine, alanine, serine) dropped below the "norm" [10]. It should be noted that, of the five amino acids whose concentration was below the "norm" [10] before the flight, three (cystine, arginine and aspartic acid) continued to decline after the flight, while two (methionine and histidine) showed a tendency toward insignificant rise or stabilization. A comparison of concentrations of amino acids in blood plasma of the CDR after the flight to the "norms" of Muller revealed that this parameter was below the usual values for 12 out of 17 amino acids (lysine, leucine, isoleucine, phenylalanine, cystine, tyrosine, alanine, arginine, histidine, glycine, proline and serine). Before the flight, only three amino acids (methionine, cystine and histidine) presented lower concentrations than the "norm" cited by Muller. Preflight concentration of glutamic acid exceeded the "norm" and after the flight it dropped to mean "normal" levels [12]. Postflight methionine content reached the "norm," histidine level rose somewhat but was below the bottom of the "normal" range, while the concentration of cystine dropped and became even lower than the bottom range of the "norm." Thus, after the flight the concentrations of most amino acids in plasma of the CDR were also below the values taken as the "norm" by Muller [12]. As compared to the mean figures cited by I. B. Zbarskiy, after the flight the concentrations of 13 amino acids were below the mean figures and only 3 amino acids (threonine, aspartic and glutamic acids) exceeded or corresponded to the mean levels [11]. Before the flight, five amino acids presented mean or higher concentrations: threonine, aspartic and glutamic acids, glycine and serine. Thus, the levels of most amino acids in blood plasma dropped after the flight in the CDR. The concentrations of most amino acids were below the bottom range of "normal levels" cited in several authoritative sources [10, 12] and below the mean figures [11]. A comparison of the data to those cited in the above sources compels us to conclude that there was worsening of plasma amino acid parameters in the CDR, as compared to his status before the flight.

Immediately after the flight, plasma levels of only three amino acids (cystine, alanine and aspartic acid) were below the "tentative data" [10] in the FLE. The concentration of threonine was above the "tentative data" levels, as was the case before the flight, but to a lesser extent (by only 0.48 mg%, versus 1.14 mg% preflight). Consequently, in the course of the flight there was some normalization of threonine concentration, while histidine content rose to the "norm" [10]. The preflight concentrations of three amino acids--cystine, aspartic acid and histidine--were below the "tentative data." A comparison

of these figures to the "norms" of G. Muller revealed that the concentration of three amino acids in the plasma of the FLE postflight was below the usual concentration for adults (lysine, cystine, alanine). The preflight concentration of cystine, alanine, histidine was below the Muller "norm" while threonine, valine and glutamic acid levels were above this "norm." The concentration of cystine and alanine, i.e., the same amino acids whose concentration was also lower than the "tentative data" [10], was low (according to Muller). On the other hand, as compared to Muller's figures, lysine content was below normal. As compared to the data of I. B. Zbarskiy, postflight concentration of 12 amino acids (lysine, valine, methionine, leucine, isoleucine, cystine, tyrosine, alanine, arginine, histidine, glycine and proline) was lower in the FLE, while 4 amino acids (threonine, aspartic and glutamic acids, serine) exceeded or corresponded to the mean values; preflight levels of 9 amino acids were lower and 7 were higher or equal to the means [12]. Thus, in the FLE also, the postflight concentrations of most amino acids were lower than preflight. However, after termination of the mission, in the FLE the concentration of only three amino acids was below the "tentative physiological norm," whereas in the CDR the levels of most amino acids became lower than this "norm." As compared to average levels of amino acids cited by I. B. Zbarskiy, the status of both cosmonauts was about the same: the concentration of 12 amino acids was low for the FLE and that of 13 was low in the CDR. Hence, it can be concluded that, although fewer amino acids of the CDR presented a postflight concentration that was lower than before the flight, as compared to the FLE, the plasma amino acids were on a lower level and most of them were below the "tentative physiological norms" [10, 12]. Dissimilar utilization of amino acids because of differences in physical work load and in inflight food intake, as well as individual metabolic distinctions, could be the causes of differences in dynamics of inflight concentrations of amino acids in the CDR and FLE. Perhaps, there were also different reactions to the set of spaceflight factors.

After termination of the flight, the sum of essential amino acids was lower than preflight in both cosmonauts: by 1.04 for the CDR and by 2.64 mg% for the FLE (see Table 2). The sum of their essential (six] amino acids also decreased: by 4.54 mg% for the CDR and 3.68 mg% for the FLE. For this reason, the overall sum of amino acids also decreased: by 5.58 mg% for the CDR and 6.32 mg% for the FLE. The proportion of essential to nonessential amino acids (E/N) changed in both cosmonauts after the flight in the direction of increase, due to relatively greater decrease in nonessential amino acids than essential ones. This ratio increased more (by 0.31) in the CDR than the FLE (by only 0.06), which is attributable to the more intensive decline of nonessential amino acids in the CDR and, at the same time, less decline of essential ones, than in the FLE.

While the difference in the individual diet in the preflight period could be significant, and this could have been the main factor in forming a relatively less favorable "amino acid status" for the CDR than the FLE, during the flight both crew members were to receive daily only food allowances that were identical in quantity and assortment of foods. We could have expected that the concentrations of amino acids would be closer in the CDR and FLE at the end of the flight, as compared to preflight values. Indeed, the difference in sums of essential and nonessential amino acids, as well as the overall sum thereof was smaller after the flight than before. Such "leveling off" was particularly

noticeable with respect to essential amino acids. However, even after the flight, the levels of most amino acids in blood plasma were higher for the FLE than CDR. The difference even increased for nonessential amino acids. One of the possible causes of the better "amino acid status" of the FLE after the flight could be that he weighed less than the CDR (by almost 10 kg preflight and 13.8 kg postflight). Consequently, during the flight, the FLE received daily somewhat more protein and amino acids in the food allowance per kg weight than the CDR. The overall energy expenditure should also have been somewhat smaller than for the CDR. As a result, conditions could have developed for constant, relatively poorer supply of amino acids inflight for the CDR, as compared to the FLE. For this reason, the expected "leveling off" of amino acid status did not occur, while the concentrations of amino acids in plasma were generally lower in the CDR after the flight, as they were before it, than in the FLE.

The results of our study of levels in blood plasma of 17 free amino acids in the crew of Salyut-6 before and after a 140-day flight enable us to conclude that the cosmonauts' diet prior to long-term missions should be subject to stricter physiological and hygienic monitoring, including determination of "amino acid status" in blood plasma. The existing preflight diet could be improved by enriching it primarily with methionine and cystine. During long-term flights, it is necessary to constantly monitor actual food intake by crew members, systematically analyze the body's supply of food amino acids, perform periodic laboratory blood tests to assay amino acid levels and make appropriate preventive corrections in the food allowance. The existing food allowances for long-term flights require refinement, in the form of increasing methionine, cystine, lysine, leucine, isoleucine, phenylalanine and tyrosine content. In assessing the nutritional value of daily food allowances, one must apparently take into consideration more strictly the individual differences in cosmonauts that influence their energy , amino acid and other nutrient requirements, and in particular their weight.

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NUTRITIONAL VALUE OF FOOD IN TUBES FOR PILOTS AND COSMONAUTS

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[Article by L. I. Kuznetsova, S. Yu. Gel'fand, I. G. Popov, L. A. Gurova and G. G. Akin'shina]

[English abstract from source] The nutritional value of new canned liquid and puree-like foodstuffs in aluminum tubes for aircraft and spacecraft pilots has been determined. The recipes and chemical composition of the food items are described. Particular attention is given to the content of amino acids, fatty acids and minerals. It is shown that canned foodstuffs are inhomogeneous in their chemical composition which is to be taken into consideration when they are used as menu items.

[Text] The need arises to use preserved liquid and pureed foods packed in aluminum tubes to provide for satisfactory nutrition of pilots and cosmonauts under some habitat conditions in the cabins of flight vehicles. For example, special "altitude" rations (onboard food allowances) are used, which consist exclusively of pureed and liquid foods in tubes [1-3] for pilots during flights when cabin pressure is 405 mm Hg or less, and they cannot remove or move the oxygen mask for even a short time. Analogous products are used for cosmonauts.

During the flights of Yu. A. Gagarin and G. S. Titov, the food allowance consisted of only liquid and pureed foods in tubes. In subsequent flights aboard Vostok, Voskhod, Soyuz and Salyut spacecraft, food in tubes was also used, and chiefly those that are usually consumed on the ground in liquid and pureed form [4-5].

There are several general specifications for food in tubes in developing and making up onboard food allowances. They must have sufficiently high energy and nutrient value, be well assimilated under flight conditions and have relatively high gustatory qualities, they must be suitable for consumption right from the package in both heated and cold form, stable during long storage without refrigerators at positive temperatures. An additional requirement for cosmonauts is that the foods must be usable in weightlessness. For pilots, food in tubes must also have a consistency that would allow them to pass through narrow tubes. One end of such a tube is screwed on the neck of the food-containing tube and the other is inserted in a valve for food intake in an

oxygen mask (or the face plate of a helmet). The previously developed preserved foods in tubes satisfied these requirements as a whole [6-8].

We submit here the results of developing new foods in tubes, technological distinctions of producing them and information about nutritional value.

Methods

New types of pureed and liquid processed food in aluminum tubes were developed with consideration of the above-listed requirements, special attention being given to their nutritional value and organoleptic properties. We took into consideration the most recent recommendations of the Institute of Nutrition, USSR Academy of Medical Sciences, with respect to optimum balance of essential nutrients in food.

In working out the technology of producing pureed foods, the technological processes of preparing raw material (sorting, washing, cleaning, cutting, blanching, mashing) used in the food industry served as the basis, with use of standard equipment of canning plants. As a result, a technological system was proposed for production and specifications documentation [11].

Such processes as chopping, mixing, adding hydrophilic thickeners in order to obtain the required consistency were very important to the technology of producing pureed foods in aluminum tubes. One of the important stages of production technology was to refine sterilization conditions that would guarantee the good quality of the products [9].

In working out the formulas for pureed processed food, we proceeded from the conventional variants that are used the most in the canning industry and public catering service for appetizers, first and second courses, and desserts, but we also took into consideration the technology of food for pilots and cosmonauts, qualitative parameters of different dishes and their typical distinctions.

We determined the optimum combination of elements of plant and animal origin for each type of preserved food.

Results and Discussion

As a result of our studies, recipes [formulas] and technology were developed for a wide assortment of processed foods in tubes: diverse first and second meat and vegetable courses for dinner, foods derived from cottage cheese, fruit and berry desserts and beverages.

The strict limitation of volume and weight for onboard food allowances made it necessary to work out items with high nutritional and biological value.

In this regard, it was of great interest to develop appetizers with high polyunsaturated fatty acid content by adding in the recipes up to 13% vegetable oil.

In the course of the studies, we determined how much oil was absorbed when vegetables were browned [sauteed], with determination of the need for additional vegetable oil in a number of dishes: 6.6% for chopped squash [zucchini], 2.3% for chopped eggplant. No oil was added to "lyubitel'skaya" appetizer [chopped vegetables],

since the required fat content (13%) was provided by the amount of oil in the fried onions (27%) and carrots (13%) [10].

In developing the recipes for first and second courses ready for consumption in both cold and heated form, a study was made for determination of quantity and composition of fats.

Butter, either firm or melted, which was present in pureed foods did not cause formation of a solid fatty film in the neck of the tube, as was observed after sterilization of other fats with higher melting points. Moreover, the flavor of preserved foods with butter was much better. However, addition of large quantities of butter impaired homogeneity of consistency (blobs of fat appeared in the tip of the tube). Technological studies established the optimum quantities of melted butter: 5-7.5% for first courses and 4-8% for second courses, depending on the meat. For preparation of patees, butter was used in amounts of 5-7%, in cottage cheese with pureed fruit--4%, which provided the required consistency of the food [6, 7].

Studies were made to develop the grinding process in order to obtain pureed canned goods of the required fineness. Previously used homogenization could not be applied here, since cosmonauts soon got tired of foods processed in this fashion. For this reason, in order to obtain the optimum particle size, we used the crusher method, with sieves with mesh size of 1.5 to 7 mm in diameter. As a result of the studies, it was determined that one must use sieves with 2 and 4 mm mesh size to grind the foods. However, the technology used to process pureed canned goods did not always assure their stability: water separated from the solid phase and there was impairment of homogeneous consistency. For this reason, a new method was developed to produce pureed canned foods, which provided for addition of a hydrophilic thickener--moisture stabilizer (flour, rice, semolina, gelatin). When the constituents were mixed, a stable homogeneous mass was obtained with uniform distribution of suspended particles. In the course of the studies determination was made of percentile amounts of thickeners for each type of food.

A new technology was developed to produce sterilized cottage cheese with fruit, which assured a long shelf life, its flavor and nutritional value were close to that of the unadulterated product, and it had optimum consistency.

The appetizers, first and second courses processed in tubes had a homogeneous consistency throughout, with insignificant separation of broth and fine pieces of some ingredients.

The flavor and aroma of these dishes were the same as in the same dishes prepared by ordinary culinary methods.

The nutritional and biological value of a product is very important to its physiological and hygienic characterization, and it is determined on the basis of amounts of biologically active substances, in particular, amino acids and polyunsaturated fatty acids, as well as minerals.

Studies of amino acid composition of proteins in canned goods by the method of ion exchange chromatography enabled us to identify and quantitatively assay

17 amino acids. Table 1 lists data on amounts of different amino acids in five types of pureed canned goods representing first and second courses, and desserts.

Table 1. Amino acid composition of five types of foods in tubes (g/100 g product)

AMINO ACID	KHARCHO SOUP*	BORSHCH	MEAT WITH VEGETABLES	PORK WITH PEPPER	COTTAGE CHEESE WITH PUREED FRUIT
LYSINE	7,70	7,76	6,77	5,12	7,0
HISTIDINE	2,36	3,75	4,50	3,01	4,32
ARGININE	6,11	6,90	4,75	4,44	2,58
ASPARTIC ACID	11,88	10,30	10,0	10,29	7,39
THREONINE	4,83	3,94	5,16	4,49	5,32
SERINE	4,74	4,80	4,48	4,73	5,43
GLUTAMIC ACID	17,85	18,05	18,32	19,99	18,90
PROLINE	6,39	4,32	4,24	4,65	6,97
GLYCINE	6,11	4,91	4,93	5,93	1,40
ALANINE	6,82	5,85	6,29	6,16	3,21
CYSTINE	0,70	1,19	—	—	1,50
VALINE	3,85	2,90	4,18	4,24	5,54
METHIONINE	2,54	1,97	2,64	1,58	1,84
ISOLEUCINE	3,26	5,0	3,93	3,65	4,25
LEUCINE	5,86	8,63	8,14	7,72	9,05
TYROSINE	4,05	5,06	3,25	3,30	7,57
PHENYLALANINE	3,77	4,63	4,05	3,93	7,04

*Translator's note: Caucasian style soup containing mutton, tomatoes, rice and seasonings.

We used the amino acid score calculated on the FAO [Food and Agriculture Organization of WHO] scale as an indicator of biological value of pureed canned foods (Table 2).

Table 2. Amino acid score of pureed food in tubes

AMINO ACID	NAME OF PUREED ITEM IN TUBE					FAO SCALE	
	KHARCHO SOUP	BORSHCH	MEAT WITH VEGETABLES	PORK WITH PEPPER	COTT. CHEESE WITH PUREED FRUIT	AMINO ACID CONTENT/100 G PROTEIN	SCORE, %
LEUCINE	84	123	117	110	129	7,0	100
ISOLEUCINE	82	125	98	91	106	4,0	100
VALINE	77	58	84	85	111	5,0	100
METHIONINE	73	56	75	45	53	3,5	100
LYSINE	140	141	123	93	127	5,5	100
PHENYLALANINE	130	161	122	121	243	6,0	100
THREONINE	121	99	129	112	133	4,0	100

According to the data listed in Table 2, we see that the processed dish, "cottage cheese with pureed fruit," is balanced in all essential amino acids (with the exception of methionine). Valine and methionine are the limiting amino acids of proteins in borshch [beet and cabbage soup], isoleucine, valine and

methionine are such factors for the rest of the products in tubes. The shortage of these amino acids does not exceed 20%. It should be noted that methionine can be arbitrarily considered a limiting amino acid in the above foods, since a considerable part of it is broken down upon hydrolysis and only the remaining amount is demonstrable on chromatograms. The score for lysine, phenylalanine and threonine exceeds 100% in virtually all of the products, which is indicative of the rather high biological value of the pureed foods.

In order to determine the ratio of essential amino acids of protein, we calculated the A/E index (in mg essential amino acid per gram total essential amino acids; Table 3).

Table 3. A/E index for pureed processed foods

AMINO ACID	BORSHCH	KHARCHO SOUP	MEAT WITH VEGETABLES	PORK WITH PEPPER	COTT. CHEESE WITH PUREED FRUIT
ISOLEUCINE	86,36	97,06	102,09	108,82	90,3
LEUCINE	148,53	164,34	212,04	226,47	191,0
LYSINE	134,72	214,48	178,01	150,00	147,0
METHIONINE	34,54	69,64	68,06	40,06	37,8
PHENYLALANINE	79,45	105,85	107,33	114,71	147,0
THREONINE	67,36	133,70	136,13	132,35	111,0
VALINE	50,09	105,85	109,95	123,53	116,0

A comparison of this index to the "ideal scales" indicates that the proteins were balanced in the tested pureed foods in tubes.

Table 4. Fatty acid and mineral content of pureed processed foods

PARAMETER	"LYUBITELSKAYA" CHOPPED VEGETABLE	KHARCHO SOUP	BORSHCH	MEAT WITH VEGET.	COTTAGE CHEESE WITH PUREED FRUIT
	FATTY ACIDS (G/100 G PRODUCT)				
CAPRIC C_{10}	—	0,32	0,21	0,04	0,20
LAURIC C_{12}	—	0,34	0,19	0,03	0,28
MYRISTIC C_{14}	—	1,64	0,92	0,42	1,62
PALMITIC $C_{16:0}$	1,09	3,7	2,37	1,45	4,80
PALMITOLEIC $C_{16:1}$	—	0,18	0,35	0,06	0,20
STEARIC $C_{18:0}$	0,56	1,08	0,77	0,57	1,31
OLEIC $C_{18:1}$	3,43	2,65	2,30	1,61	3,33
LINOLEIC $C_{18:2}$	5,28	0,34	0,27	0,15	0,34
LINOLENIC $C_{18:3}$	0,22	0,16	0,18	0,06	0,22
	MINERALS (MG/100 PRODUCT)				
Ca	38,5	18,8	25,3	19,1	80,0
Mg	22,7	37,3	58,5	14,7	26,1
P	56,2	71,1	74,9	38,7	117,8
Fe	3,25	4,10	4,0	2,45	1,20
K	152,1	79,6	116,9	109,3	100,9
Na	437	360	531	424	93

In assessing whether the food allowance is balanced, the fatty acid content of food lipids is very important. With the method of gas-liauid chromatography, nine fatty acids were identified in processed food lipids and they were assayed (Table 4).

The studies revealed that"lyubitel'skaya appetizer [chopped vegetables], in the recipe for which vegetable oil was included, could serve as one of the main sources of polyunsaturated linoleic acid in the diet. Having one tube of "lubitel'skaya" in the diet satisfies the daily human requirements with regard to essential polyunsaturated fatty acids.

The other pureed processed foods cannot serve as a source of polyunsaturated fatty acids, and this must be taken into consideration in providing the daily food allowance.

Much attention is given to studies of mineral content (these studies were made by the method of atom-absorption spectrometry; the results are listed in Table 4).

As can be seen in Table 4, the assayed items are important sources of minerals in the diet of pilots and cosmonauts. Moreover, a good proportion of calcium and phosp orus was found in the cottage cheese with pureed fruit, which is instrumental in easy and high assimilation of calcium.

The results of our study revealed that the chemistry of processed foods in tubes is heterogeneous and their nutritional value differs. Some items are richer in amino acids, others in fatty acids, others yet in minerals, etc. All this must be taken into consideration when working out food allowances for pilots and cosmonauts, in particular, the chemical composition of other food items that may be used in the future or recommended for inclusion in specific flight diets. The distinctions of chemical composition of processed foods in tubes must also be taken into consideration in organizing preflight and postflight meals.

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UDC: 613.693-07:616-056.257-07

PHYSICAL STATUS AND BIOCHEMICAL PARAMETERS OF OBESE PILOTS AFTER IMPLEMENTATION OF PREVENTIVE MEASURES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 6 Apr 82) pp 35-37

[Article by H. Lyson-Wojcechowska, M. Pendziwiatr, Z. Koter and K. Kwarecki (Polish People's Republic)]

[English abstract from source] This paper presents the results of comprehensive examination (medical, anthropological, biochemical investigations and exercise tests) of obese pilots treated in specialized centers to make them lose weight.

[Text] Obesity is particularly detrimental in flight work, since it lowers endurance of such flight factors as accelerations, hypoxia, vibration and others. Obesity has an adverse effect on work capacity and physical activity of pilots [1, 2], it increases the risk of a number of diseases and, consequently, of grounding pilots.

Some of the metabolic and biochemical disturbances associated with obesity are the same as those found in the presence of atherosclerosis and diabetes mellitus [3, 4]. There are reports in the literature to the effect that these disturbances revert to normal after weight loss.

The results of studies conducted in this area revealed that 33% of the pilots are overweight and 17-18% are obese [5], which is higher than the parameters for other occupational groups. For this reason, a set of preventive measures is used extensively in the Polish People's Republic. In addition to monitoring composition of food, work-up at a hospital and treatment, special measures are instituted to reduce weight and educational-conditioning centers.

We submit here the results of comprehensive studies of obese pilots who were at two educational and conditioning centers.

Methods

We examined obese pilots who were referred to the educational-conditioning centers by an internist and anthropologist in the course of an expert examination.

Obesity was diagnosed when body weight exceeded by 15 and 20% the figure recommended by Weslaw [6]; it was referred to as moderate and severe according to the obesity nomogram for flight personnel [7].

The store of fat was assessed on the basis of measurement of subcutaneous fatty tissue, measured with a fold gauge used in 2 or 10 diagnostic points according to Parizkova.

Each group (shift) of pilots spent 3 weeks at the center. Educational and physical culture exercises were scheduled in relation to average load levels.

The diet used consisted of about 2251 kcal. Pastry, sweets, jam and fruit puddings were excluded from the diet. Foods containing flour, potatoes and cereals were markedly restricted. There was no radical reduction in fat intake, particularly vegetable oil, which, in spite of their high caloric value, are a rich source of a number of nutrients, including unsaturated fatty acids. Table 1 lists the chemical composition of the diet used for the pilots treated at the conditioning centers.

Table 1. Chemical composition of diet

TIME	CALORIES	PROTEIN	FATS	CARBO-HYDRATES	CALCIUM	VITAMIN C
BREAKFAST	762,2	34,2	34,5	78,7	404	10
LUNCH	752,1	18,3	32,8	45,8	90	11
DINNER	947,0	43,0	34,2	116,8	223	135
SUPPER	777,2	27,2	34,1	90,3	137	28
AVERAGE	2251,7	110,2	108,8	207,8	764	150

Results and Discussion

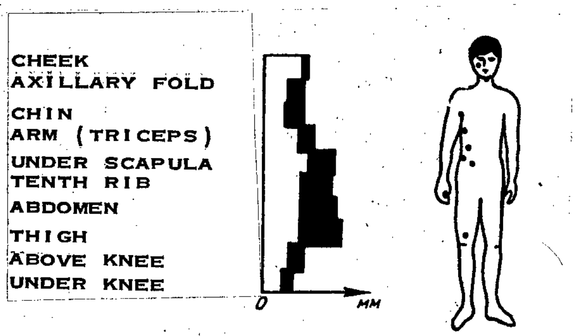
Already after a 3-week period on the diet and increased exercise, there was a marked decline of biochemical parameters of blood serum in obese pilots: glucose by 4.4 mg%, total lipids by 82.1 mg%, β-lipoproteins by 28.2 mg% and triglycerides by 103.9 mg%. Table 2 lists average levels of the biochemical parameters assayed and percentile change in parameters after termination of the stay at the center of the shift of pilots referred there to lose weight.

Analysis of glucose and insulin curves enabled us to detect 3 cases (11% of the total number of subjects) of impairment of carbohydrate metabolism, and it was significantly improved toward the end of the stay.

The tested group of obese pilots presented the typical adiposity parameters of obese individuals. Mean fat content was determined on the basis of reserve of subcutaneous fatty tissue. It constituted 17-18% (from 14 to 24%) in obese pilots and statistically different appreciably from fat content in pilots in general--about 13% (from 11 to 15%). The distribution of subcutaneous fatty tissue in obese pilots at 10 typical points, as compared to the general population, is illustrated in the Figure.

Table 2.
Mean values of biochemical parameters (mg%) in blood serum of obese pilots

BIOCHEMICAL PARAMETER	START OF SHIFT	END OF SHIFT	% CHANGE
GLUCOSE	86,0	78,6	8,6
TOTAL LIPIDS	731,0	648,9	11,2
β-LIPOPROTEINS	153,7	125,5	18,3
TRIGLYCERIDES	233,2	129,3	44,6



Distribution of subcutaneous fatty tissue in obese pilots at 10 diagnostic points, as compared to the general pilot population
Light portion refers to general population and black, to obese pilots

The average age of obese pilots at the first center was 36 years (25 to 56 years) and in the second, 30 years (22 to 44).

After a 3-week stay, the group that was to lose weight presented reliable changes in some morphological and physiological parameters.

In both groups, weight loss constituted 1.75 kg (0.3 to 4.5 kg), but the drop was unreliable.

There was a reliable decrease in fat content: by one-third in relation to body weight (about 7%) in obese pilots at the first center and one-fifth in relation to body weight of obese pilots at the second one (about 10%).

A statistically significant increase in body firmness after staying at the center is a manifestation of favorable changes in proportions of fat and mass of active cells.

The greatest changes were observed in subcutaneous fatty tissue in the region of the abdomen and 10th rib (13 and 15%, respectively, of fatty tissue loss). A large reduction of subcutaneous fat was also noted on the posterior aspect of the thigh and over the biceps (about 10% change).

Concurrently, there was statistically significant increase in relative mass of active cells, more marked in pilots at the second center (about 2.5% change) than those at the first one (about 1.4% change), which is also indicative of favorable changes in body schema proportions.

Of the results of the physiological tests, the substantial increase in oxygen uptake (consumption), with respect to both mass of active cells and body surface (about 8-9% change), merits attention.

The age factor and its inherent dynamics of progressive change in different anatomical properties [8] were of deciding significance to the more intensive rate of development of changes (increase or decrease of a given property), in the relatively younger group of pilots at the second center (average age 30 years) than in the pilots from the first center (average age 36 years).

During the growth period, one can obtain more significant changes in morphological properties than in the subsequent stable period; for this reason, preventive measures should be instituted primarily for obese pilots of a younger age.

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EFFECT OF SEVEN-DAY SPACEFLIGHT ON STRUCTURE AND FUNCTION OF HUMAN LOCOMOTOR SYSTEM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 5 May 82) pp 37-44

[Article by R. Hernandez-Korwo, I. B. Kozlovskaya, Yu. V. Kreydich, S. Martinez-Fernandez, A. S. Rakhmanov, E. Fernandez-Pone and V. A. Minenko (Republic of Cuba and USSR)]

[English abstract from source] The goal of the joint USSR-Cuba experiment, Support, was to study the support properties of the foot arch in weightlessness-induced motor changes and their prevention with the help of the Cupula Sand-501 device. Comparison of the responses of the crewmembers shows that support simulation diminished the level of many of the adverse effects of zero-g in the Cuban pilot who used the prophylactic device. It is suggested that the efficiency of the device is due to its activation of the system of support reactions. The mechanisms of the effects of weightlessness on the structure and function of the bones and joints in humans are discussed.

[Text] Impairment of functions of the skeletomuscular system [locomotor system] occupies an important place among the disorders caused by diminished gravity. Man and animals have shown a decline of muscle tone, impairment of vertical stability, change in structure of locomotor acts, muscular atrophy and other motor deviations under the influence of weightlessness and conditions that simulate it [1-7].

Apparently, the decrease in static load and related change in influx of support afferentation, which plays an important role in maintaining the tone of postural muscles and, in particular, muscles of the leg and foot, is one of the causes of the above changes during short-term flights. Changes in structure and functions of the support system of the foot, due to diminished rigidity of crural and foot muscles, may be an additional factor causing development of motor disturbances.

Proceeding from these conceptions, as well as the results of previous joint Soviet-Cuban model studies (7-day immersion), Cuban specialists developed a method for studying the role of changes in the arch of the foot in development of motor disturbances caused by weightlessness.

Our objective was to investigate the effect of weightlessness on structure and functions of the human support system, demonstrate the role of changes in support properties of the foot in the pathogenesis of motor disturbances caused by weightlessness, study the possibility of preventing changes elicited by weightlessness in structural and functional properties of the foot and other motor disturbances.

These studies were conducted aboard the Salyut-6 station during a joint mission by a Soviet-Cuban crew.

Methods

The Cuban cosmonaut (CC) had to daily wear on both feet the special "Cupula SAND-501" gear, which consists of sandals with spring-loaded insole, in the cuff of which excess pressure was created with a rubber bulb and manometer, and it was possible to regulate it in the range of 20 to 60 mm Hg, and it could be worn for 4 h. Air pressure in the cuff, which was determined by the cosmonaut, was not to be less than 15 mm Hg. The Soviet cosmonaut (SC) did not use this gear.

The state of the skeletomuscular system was examined 10 days before the flight (background data), as well as on the 1st and 3d postflight days. To assess the functions of the locomotor system and preventive effect of the gear, we used a standard set of methods proposed by Soviet specialists [7], which included determination of sensitivity to vibration of support zones of the foot, reflexometry (tendinal, T reflex) and isokinetic dynamometry of crural muscles. On the Cuban side, the studies were supplemented with several new methods for detailed examination of properties of the support system of the foot. These methods involved implementation of the following measures: 1) plantography with detailed analysis of several biomechanical characteristics--width of metatarsus (a), maximum diameter of tarsus (b), projection of internal (c) and external (d) longitudinal arches of the foot, width of heel support (e) and others (Figure 1A); 2) roentgenography of the foot with subsequent measurement of parameters characterizing size of arch at rest (without load--WL) and with load: angles of internal and external arches of the foot (angles *1* and *2*), height of internal arch (h_1), height of external arch (h_2), distance between sustentaculum to calcaneus from angle *1* (g), distance between sustentaculum of calcaneous and bearing point of the first toe (i) (Figure 1B).

A load equal or exceeding body weight was created under conditions when the subject shifted his weight to the foot of one leg (body mass proper--MP) or with an additional weight (AW) in the hands (8.5 kg). All films were taken at a distance of 75 cm in the lateral projection focused on the level of the talonavicular joint; 3) 6-point stabilography to assess loads on different regions of the foot and projection of general center of gravity (GCG). Six-point stabilography differs from the usual in that there is considerable reduction of support area and, consequently, complication of the task. The results of the 7-day immersion study revealed that, while under conditions of standard stabilography changes in regulation of posture were demonstrable only with readings taken over periods of a minute [or minutes], with 6-point stabilography 10 s were enough to obtain distinct results. The studies were conducted with and without visual monitoring, using a 6-point stabilograph, on the platform of which the subject stood barefoot for 10 s. Values on the stabilogram curves

were measured every 0.2 s. The obtained data were processed on a computer on a specially prepared program, which provided for computation of means, minimum and maximum values at each support point, overall size of anterior, posterior, left and right distribution of body mass and overall mass, as well as projection of GCG and its fluctuations; 4) cinecyclography of walking, which was performed by the standard method that did not differ appreciably from the classical method developed by N. A. Bernshteyn. Films were taken in lateral projection at a distance of 5.26 m, with objective at 1 m and range of displacement of the subject of 3.3 m, at the rate of 32 frames/s. The tested modes included ordinary walking and with an additional weight (8.5 kg) in the hands. The frames were analyzed on special precision equipment with output to a digital printer. On the basis of the obtained data, graphs were plotted of angular velocities, accelerations and motion in the joints of the lower extremities.

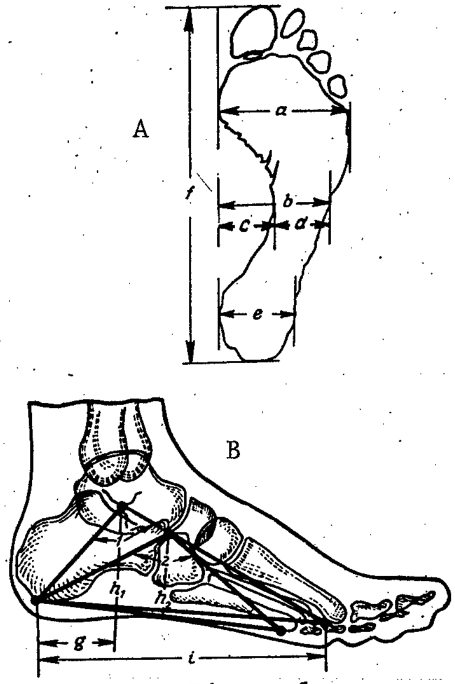

Figure 1.
Analyzed parameters of plantogram (A) and roentgenogram (B). Explained in the text.

Results and Discussion

During the flight, the Cuban cosmonaut adhered to the study conditions in a somewhat altered mode; he increased the intensity and time of applying pressure to the foot from 20 mm Hg for 4 h on the 1st day to 60 mm Hg for 6 h on the 3d-4th days of flight and thereafter. The latter was related to the fact that on the very 1st day of flight there was inhibition of spatial illusions in this cosmonaut with use of the insoles. According to his verbal account, raising pressure in the cuffs of the gear was associated with appearance of a heavy sensation in the lower limbs and rapidly led to disappearance of illusion of turning upside down. Appearance of sensation of "top and bottom" facilitated orientation considerably, as well as movement and work on the station. The illusions reappeared 1-2 h after taking off the gear.

Sensory systems. As shown by the background studies, threshold levels of vibration sensibility of support zones of the feet of both cosmonauts were in the range of +15–+20 dB for all frequencies of vibrostimulation, which corresponded to the mean statistical normal range. After the flight, the SC presented distinct increase (by more than 3 times) in sensitivity to vibration, which was manifested by a decline of perception thresholds in all support zones. The averaged changes in sensitivity to vibration of different zones were the most marked at frequencies of 63 and 125 Hz (Figure 2a). Conversely, in the CC, there was substantial rise of thresholds and decline of vibration sensitivity (by 1.5-3 times) at frequencies of 63 and 250 Hz in all tested zones.

Postflight, both cosmonauts also presented some elevation of thresholds of muscle sensitivity. In the SC, the thresholds of tendon reflexes rose from 800 g to 100 g and in the CC from 200-300 g to 600 g (Figure 2b). The change in muscle sensitivity was associated with marked (average of 25%) decrease in amplitude

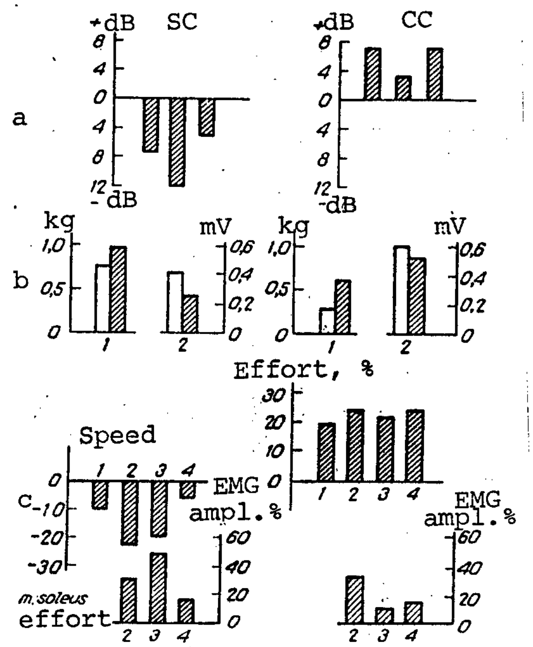

Figure 2.
Effect of 7-day flight on change in characteristics of supporting (a; according to thresholds of sensitivity to vibration, in dB, in relation to background), muscular (b; according to parameters of Achilles T reflex) afferent inputs and velocity-force characteristics of the posterior group of crural muscles (c; according to isokinetic dynamometry, % of background).
White bars--preflight; crosshatched--postflight.
In b: 1) threshold of T reflex
2) maximum amplitude
In c: 1-4) rates of 0.60, 120 and 180 degrees/s

of response of the gastrocnemius in all sensitivity ranges. Maximum amplitude of SC responses was drastically diminished (see Figure 2b). Both cosmonauts presented inhibition of interextremity reflex interactions; voluntary extension of the gastrocnemius (posterior flexion) of the contralateral leg, which had elicited depression of the reflex before the flight, now had an insignificant effect on its amplitude.

Crural muscular system. In the SC, 7-day weightlessness elicited a change in velocity and force properties of leg muscles. After the flight, isokinetic dynamometry demonstrated a considerable decrease in his maximum moments of force of the gastrocnemius at all specified rates of movement, with maximum changes when working in modes of 120 and 60°/s (25 and 20%, respectively), associated with considerable (up to 50%) increase in amplitudes on the electromyogram (EMG) (Figure 2c).

In the CC, the force characteristics of the gastrocnemius and anterior tibial muscle after the flight were, on the contrary, somewhat greater over the entire tested range--in isometric mode there was a 20% increment in muscular strength, with insignificant changes in EMG amplitudes (see Figure 2c).

The reproduction of precision, graded (30% of maximum) exertions was impaired in both cosmonauts: errors in reproduction constituted 15-20%, and they were distinctly demonstrable with exertion of both the anterior tibial muscle and the gastrocnemius.

Support system. According to plantographic data, the flight did not contribute major changes in the plantogram characteristics of the CC and did change them somewhat in the SC. As can be seen from the data in Table 1, the SC presented postflight reduction in length (*f*) of both feet (by 7 and 4 mm) and width of the tarsus (*b*, by 1 mm). Parameter *a-c* on the plantogram (see Figure 1A), which reflects the size of the arch, was also diminished on the right foot by 4 mm.

Analysis of x-ray parameters revealed that the changes in plantogram characteristics indicative of increase in accentuation of the arch and some decrease in its rigidity could be related in the SC to insignificant increase in contact reactivity

of the foot. With the change from rest to a load (WL and MP, Table 2) there was more significant decrease in angle *1* in the SC after the flight (-5°) than before the flight. The height of the internal arch h_1 (see Figure 1B) was virtually unchanged; however, parameter g, which remained more or less stable in the left foot, shifted about 5 mm back in the right.

Table 1. Plantogram parameters (in mm)

SUBJECT AND TIME OF STUDY	*a*	*b*	*c*	*a—c*	*d*	*e*	*f*
SC:				RIGHT FOOT			
BEFORE FLIGHT	76	92	38	54	38	54	241
1ST POSTFLIGHT DAY	77	90	40	50	37	52	234
3D POSTFLIGHT DAY	78	91	38	53	40	52	240
				LEFT FOOT			
BEFORE FLIGHT	77	89	36	53	41	55	241
1ST POSTFLIGHT DAY	76	87	32	55	44	56	237
3D POSTFLIGHT DAY	77	88	33	55	44	55	238
CC:				RIGHT FOOT			
BEFORE FLIGHT	73	83	37	46	36	55	257
1ST POSTFLIGHT DAY	75	84	36	48	39	53	256
3D POSTFLIGHT DAY	73	83	38	45	36	53	256
				LEFT FOOT			
BEFORE FLIGHT	75	86	37	49	38	58	257
1ST POSTFLIGHT DAY	72	83	35	48	37	54	256
3D POSTFLIGHT DAY	70	83	38	45	32	53	266

A comparison of data obtained with both methods shows that the anterior zone of the metatarsus is the center of change in the feet in the SC following the flight. On his postflight x-ray, there was a shift of the navicular bone (and, with it, of the anterior and second cuneiform bones) and marked lowering of the rest of the functional line of the foot, which apparently explains the noticeable width of the tarsus, relatively narrow arch and small area of heel print inherent in this cosmonaut.

According to the roentgenological findings, the flight elicited in the CC some flattening of the foot, as indicated by increase in h_1 and h_2. This was not associated with change in reaction to a load, and functional linearity of the foot was completely intact.

Regulation of pose. Studies of pose and distribution of loads over different parts of the foot revealed that the flight did not elicit any appreciable changes in the stance of the CC. Postflight projections of the GCG, when measurements were taken with the eyes open and shut, presented the same coordinates

in this cosmonaut (Table 3). The fluctuations of the GSG did not exceed preflight values.

Table 2. X-ray parameters

TIME	PARAMETER	ANGLE 1 DEGR.	ANGLE 2 DEGR.	h_1 MM	h_2 MM	g MM	l MM
	SC (LEFT FOOT)						
BEFORE FLIGHT	WL	115	116	40	40	34	158
	MP	112	115	40	40	35	158
	AW	116	119	40	40	35	167
1ST POSTFLIGHT DAY	WL	117	115	40	40	35	162
	MP	112	117	40	40	32	160
	AW	114	119	40	38	35	160
	CC (LEFT FOOT)						
BEFORE FLIGHT	WL	108	122	44	37	37	155
	MP	114	127	42	33	39	160
	AW	114	128	42	33	40	162
1ST POSTFLIGHT DAY	WL	112	126	43	34	38	155
	MP	113	129	41	32	39	162
	AW	116	130	41	32	41	162

Table 3. GSG projection (coordinates of axes, arbitrary units)

SUBJECT	TIME OF STUDY	FREE STANCE							
		EYES OPEN				EYES CLOSED			
		TO RIGHT	TO LEFT	FORWARD	BACKWARD	TO RT	TO LEFT	FORWARD	BACKWARD
SC	1 DAY BEFORE FLIGHT	—	1,4	9,2	—	2,8	—	16,2	—
	1ST POSTFLIGHT DAY	—	5,0	3,3	—	—	3,3	—	3,1
	3D POSTFLIGHT DAY	1,9	—	—	0,2	2,8	—	—	3,7
CC	1 DAY BEFORE FLIGHT	1,8	—	—	10,8	2,0	—	—	10,0
	1ST POSTFLIGHT DAY	1,6	—	—	9,0	2,0	—	—	7,0
	3D POSTFLIGHT DAY	3,1	—	—	9,0	4,0	—	—	7,2

In the SC, the flight caused an obvious shift backward of the GSG, which became more marked when visual monitoring was excluded (see Table 3). There was more marked increase in amplitude of GSG fluctuations, which also persisted on the 3d postflight day.

Analysis of distribution of body mass over different bearing points of the foot revealed that the SC presented an "anterior stance" with increased load on the external margin of the arch (points *3* and *6*); in the CC, the main load was on the posterior support points (*1*, *4*) with relatively uniform distribution of mass over the anterior points (Figure 3). On the whole, the flight did not alter the stance features inherent in each cosmonaut: the SC presented relative increase in load on posterior points (*1*, *4*), whereas in the CC there was no appreciable difference in distribution of load (see Figure 3).

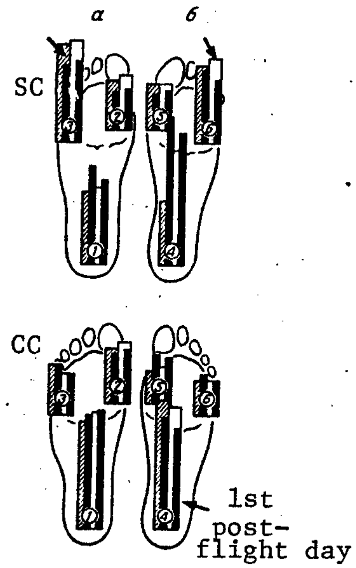

Figure 3.
Distribution of mass over main bearing zones of the foot (indicated by numbers) before and after flight
White bars--free stance with eyes open, crosshatched--with eyes closed; black bars--1st postflight day (calibration 2 kg)

Analysis of cinecyclograms of walking was impressive in that there was a difference in motion stereotypes of the cosmonauts in the preflight period. The tendency toward greater support to the front and, consequently, to some overloading of the tarsal zones of the foot of the SC caused a typical feature in his gait: smaller angle in the ankle and knee joints (119 and 93°, versus 137 and 99° for the CC) and marked rocking from side to side. The trajectories of displacement of articular centers of the lower limb during walking were characterized in this cosmonaut by marked drop of the articular center of the pelvis and knee joint at the time of bearing on the foot; in the CC, the trajectories of displacement presented a more uniform curvature Figure 4A).

In both crew members, the flight caused changes in all examined characteristics of the cinecyclogram of walking, but the extent of these changes was appreciably greater for the SC. After the flight, he presented a distinct tendency toward increase in angular amplitude of motion in the knee and ankle joints, with considerable increase in developed vertical accelerations (Figure 4B). These disturbances persisted even on the 3d postflight day. In the CC, the changes in parameters of walking cyclograms were relatively minor.

Examination of the dynamics of changes in angles in the knee and ankle joints in the postflight period revealed better organization and stability of these parameters in the CC. The first postlanding day was found to be critical for both cosmonauts (with minimal angle of flexion).

The results of this study enabled us to draw some preliminary conclusions as to the genesis of motor and sensory effects of weightlessness and possibility of preventing them.

According to individual comparison of parameters referable to motor activity in both cosmonauts, simulation of inflight support diminishes the severity of a number of adverse effects of weightlessness: in the CC, who had flown for the first time but used the preventive gear in flight, the changes in velocity and force properties of the crural muscles, postural and locomotor disturbances usually observed after flights of such duration were less marked than in the SC, who already had experience with spaceflights, or else were not manifested at all. It can be assumed that the efficacy of the gear used in flight is related to activation of the system of support reactions, which play an important role in regulating muscle tone and mechanisms of postural and locomotor control [8].

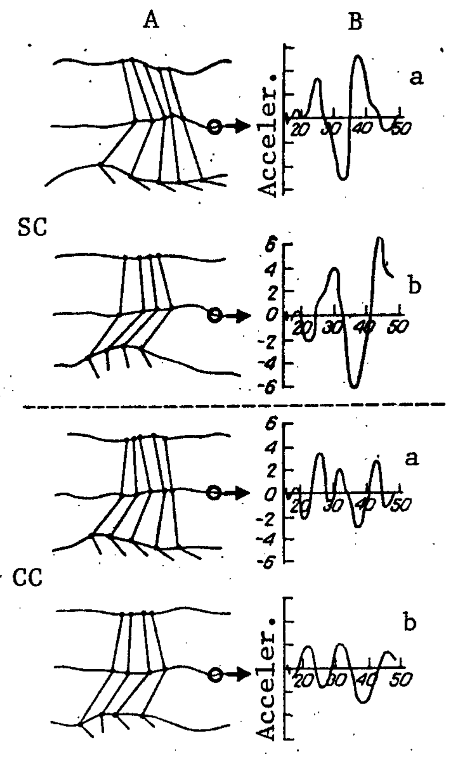

Figure 4.
Cinecyclograms of walking (A) and vertical acceleration of motion (in degrees/s^2) in the knee joint (B) before and after flight
a) background
b) 1st postflight day
Arrowhead indicates trajectory of knee joint motion

As shown by the results of the study with immersion-induced hypokinesia, removal of static loads is associated in man with marked decrease in transverse rigidity of muscles involved in maintaining an erect position both at rest and during maximum tension. In turn, this decrease in rigidity could cause a number of motor effects, in particular, a decrease in maximum force of muscular contractions, decreased rigidity of the muscular skeleton and, consequently, complication of processes of regulating erect position and walking, which have been observed under hypokinetic and weightless conditions.

The disturbances referable to vertical stability and locomotion following spaceflights could also be related to changes in properties of mechanoreceptor system of the feet, which plays an appreciable role in mechanisms of postural locomotor regulation. Under normal conditions, the support receptor system is so adjusted that average physiological loads on the foot conform to the linear range of load characteristics of receptors. This range and its threshold values are determined by the state of the receptor and tissues around it. Changes in the threshold are usually associated with a shift in range of physiologically permissible loads [9] and, accordingly, worsening of quality of regulation of processes based on this reception. As shown by the results of our investigation, in the SC weightlessness elicited a decline of thresholds of sensitivity to vibrations of support zones of the foot, and this had been observed previously in other crews of spacecraft [7]; in the CC, the thresholds of vibration sensitivity not only failed to decline after the flight, they even rose.

The effectiveness of sensory effects of the gear used by the CC is confirmed by inhibition of spatial illusions, which was observed when he wore it.

With reference to this result of our study, we should discuss briefly three distinctive features of an effect demonstrated in flight, which are of some theoretical and practical interest: a) as indicated by the CC, the efficacy of the gear diminished from day to day and, while illusions disappeared at 20 mm Hg on the 1st day, such an effect was obtained on the 3d-4th day at a pressure of 60 mm Hg. Apparently, the prolonged daily effects on the foot were associated with development of sensory habituation, which eliminated the response to insignificant stimuli; b) the inhibitory effect of the gear persisted for

1.5-2.5 h after pressure was removed from the foot, and this is apparently related to the property of retention of sensory traces, which is inherent in systems of sensory integrations; c) in the CC, the spatial illusions were characterized by early onset and inhibition, which appeared within the very first hours and persisted to the last day of the flight, unlike the usual inflight dynamics of their development. It can be assumed that the support stimuli that were used retarded processes of sensory adaptation to weightlessness, which are related to change to a visual input of systems of spatial orientation.

The factor used, which modulated some effects of weightlessness, did not change others and accentuated others yet. As can be seen from the submitted data, effects related to influence on muscular reception were among the unmodulated ones: the changes in parameters of tendon reflexes and precision characteristics of voluntary movements of the cosmonauts were identical, and they did not differ from those usually observed following flights of this duration. The accentuated effects were attributable to mechanical influences (we can include among them the tendency toward talipes planus).

In conclusiion, it should be noted that all of the above arguments can and must be taken as strictly preliminary, since they were based on the results of comparing findings referable to only two individuals, who differed not only in gear used in flight, but in the set of background signs, degree of conditioning, individual endurance etc. Apparently, sufficient data must be accumulated to single out the important effects of the above preventive gear in order to draw definitive conclusions.

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POSTURAL HEMODYNAMIC CHANGES FOLLOWING SHORT-TERM SPACEFLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 2 Apr 82) pp 44-48

[Article by T. D. Vasil'yeva, Kh. Kh. Yarullin and V. I. Zhuyko]

[English abstract from source] Variations in the pulse blood content and tone of cerebral vessels, vertebrobasilar system, lungs and legs during the antiorthostatic tests were examined rheographically in 14 cosmonauts after 8-day space flights. The results of adaptation of the vascular system to zero-g which included smaller changes in hemodynamic parameters of the hemispheres and vertebrobasilar system during postflight tests were seen during the first days of the recovery period. Regional hemodynamic parameters returned to the preflight level within 3 to 14 days postflight. The vascular response to the head-down tilt at -15 and -30° was the most informative. This led to the recommendations concerning modifications of antiorthostatic tests to be used in the selection of space crewmembers for short-term flights.

[Text] At the present time, wide use is made of the antiorthostatic [head-down] test in space medicine [1-4]. It is used in screening cosmonauts for the purpose of determining resistance of the circulatory system to changes in gravity, in the preflight period to condition the vascular system for subsequent weightlessness and in the postflight period in order to determine the extent of adaptation to spaceflight conditions.

This article deals with investigation of the dynamics of recovery from changes in filling and tonus of vessels of the cerebral hemisphere, vertebrobasilar system, right lung and right leg, which arose as a result of spaceflights lasting up to 8 days, determination of vascular regions subject to the greatest change during spaceflights, identification of the most informative parameters of regional rheograms in antiorthostatic tests (AOT) following spaceflights.

It was also interesting to analyze the reactions of the vascular system to various antiorthostatic loads in order to correct the test used in preflight and postflight expert examinations.

Methods

We analyzed the regional hemodynamic reaction to antiorthostatic tests in 14 cosmonauts who had been on spaceflights lasting up to 8 days.

The AOT involved stepped increase in load: tilting the head end of the tilt table to -15 and -30° for 6 min in each position and to -45° for 2 min. Before and after the tilts, we recorded rheograms with the patients in horizontal position. During tilts, tracings were taken in all odd-numbered minutes of the test.

We recorded the rheoencephalogram (REG) in the frontomastoid and bimastoid leads, rheograms (RG) of the right lung and right leg. A 4-channel 4RG IM rheograph was used to record rheograms. The working frequency of the rheograph constituted 120 kHz, with current of 2.5 mA and voltage of 3 V. The method for analysis of the RG was described previously [5].

Results and Discussion

Before the flights, during the AOT we observed increase in pulsed filling of vessels of the right hemisphere by an average of 76.4% with the head end of the table tilted down -15°, by 103% at -30° and by 153.7% at -45°, as compared to horizontal position ($P<0.001$; Figure 1a). On the day they landed, there was less marked increased in pulsed filling, constituting +54.7% at -15°, +84.9% at -30° and +140% at -45° ($P<0.001$). The lowest increase in parameters of pulsed filling was noted in the AOT on the 3d day of the recovery period (the increase constituted 56.5% at -15°, 82.7% at -30° and 105.8% at -45°; $P<0.001$). On the 14th day of the AOT, pulsed filling parameter was close to preflight values.

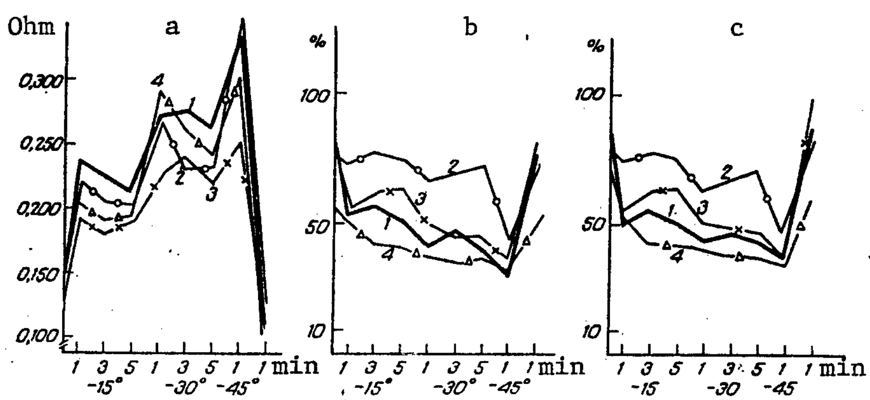

Figure 1. Changes in maximum amplitude (a), dicrotic (b) and diastolic (c) index of REG of cerebral hemispheres during AOT

Here and in Figures 2 and 3:
1) preflight
2) day of landing
3, 4) 3d and 14th postflight days, respectively

The indicator of tonus of large and medium-sized arteries ($\frac{\alpha}{T}\%$) on the REG of the right hemisphere in the preflight AOT increased by 55.6% in the 1st minute in the -15° position and remained on this level at -30° and -45°. This parameter

reverted to the preflight value immediately after the subject returned to horizontal position. There were no reliably demonstrable postflight differences in dynamics of $\frac{\alpha}{T}\%$ in the AOT, as compared to preflight values.

The indicator of tonus of small arteries and arterioles of the hemispheres--dicrotic index of the REG (DCI) dropped by 36.6% before the flight at -15°, by 50% at -30° and by 64% at -45° ($P<0.001$). During the AOT on day of landing (see Figure 1b) such a decline of DCI was not demonstrable. It is only at -45° that there was a 44% decline of DCI ($P<0.001$). On the 3d day, DCI was higher at -15° than preflight, while in other antiorthostatic positions the indicator of arteriolar tonus did not differ from preflight values. There were similar dynamics to the indicator of tonus and pulsed filling of veins of the right hemisphere during the AOT at different times following the spaceflight (see Figure 1c).

Pulsed filling of vertebrobasilar system vessels in the preflight AOT (Figure 2a) increased by 110% at -15°, 168% at -30° and 184% at -45° ($P<0.001$). On the day of landing and 3d postflight day, there was less marked increase in pulsed filling during the AOT, constituting +50% at -15°, +75% at -30° and +162% at -45° ($P<0.001$). On the 14th day, the dynamics of mean values of pulsed filling of the vertebrobasilar system during the AOT were close to preflight levels.

There was some increase in preflight $\frac{\alpha}{T}\%$ on the REG of the vertebrobasilar system during the AOT, particularly with a -45° tilt. When patients were moved to horizontal position, we observed an appreciable decline of this parameter. Such dynamics of $\frac{\alpha}{T}$ were also demonstrable at different postflight stages.

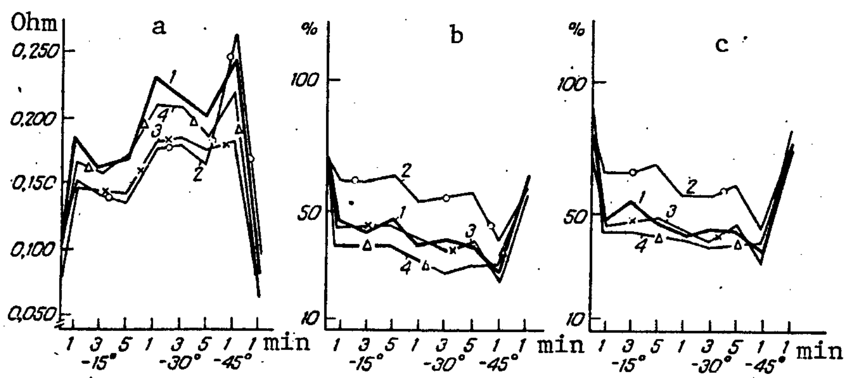

Figure 2. Changes in maximum amplitude (a), dicrotic (b) and diastolic (c) index of bimastoid REG during AOT

The DCI of the bimastoid REG during AOT dropped by 33% at -15°, 46% at -33° and 59% at -45° ($P<0.001$; Figure 2b). The postflight dynamics of the DCI during the AOT differed from preflight only on landing day ($P<0.05$) and consisted of a lesser decline of parameters of arteriolar tonus with the patients in antiorthostatic position. On the 3d day, there were no reliable differences in changes in the vertebrobasilar system DCI, as compared to preflight studies.

Similar dynamics during postflight AOT were demonstrable with reference to parameters of venous efflux and tonus of vertebrobasilar veins (Figure 2c).

Hemodynamic parameters of the lung changed insignificantly during the AOT, both before and after spaceflights. We should only mention an increase in tonus of large and medium-sized arteries, which was noted immediately after the flight, before and during AOT.

Pulsed filling of the leg (Figure 3a) in the preflight AOT increased insignificantly, and it was particularly noticeable at -45°. On landing day, parameters of pulsed filling during AOT were lower and differed reliably from preflight values at -30° and -45° ($P<0.1$ and $P<0.01$, respectively). By the 3d day, these changes leveled off and the parameters virtually failed to differ from preflight values.

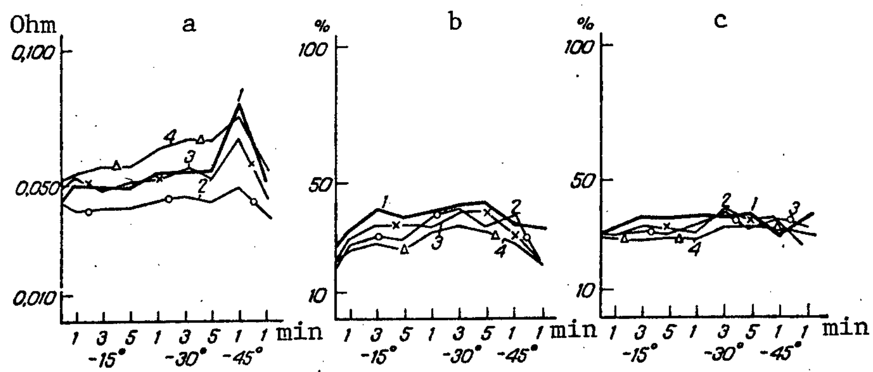

Figure 3. Changes in maximum amplitude (a), dicrotic (b) and diastolic (c) index of crural RG during AOT

In the preflight AOT, $\frac{\alpha}{T}\%$ of the leg gradually increased in accordance with increase in tilt angle. After the spaceflight, average parameters of tonus of large and medium-sized arteries before and during AOT were higher than preflight ($P<0.05$). On the 3d day, an elevated $\frac{\alpha}{T}\%$ still persisted, and it came close to the preflight level only by the 14th day.

DCI on the crural RG before the spaceflight increasing during the AOT by 54% at -15°, 100% at -30° and -45° (Figure 3b). Analogous changes were observed at different postflight periods.

The changes in crural DCI on the REG during AOT were insignificant and unreliable, both before and after spaceflights (Figure 3c).

Thus, during stepped increase in tilt angle of the AOT, there were demonstrable dynamics to parameters of filling and tonus on hemisphere and bimastoid REG's, RG of the lung and lower leg. The changes in parameters, both before and after spaceflight, were more marked in the cerebral hemispheres. Pulsed filling of the hemispheres and vertebrobasilar system after spaceflights increased less in response to antiorthostatic position than before them, which could be attributed to manifestation of adaptive and compensatory mechanisms in cerebral vessels which had developed during spaceflights in relation to intensified influx of blood to

the brain in weightlessness. Interestingly, the least increase in pulsed filling of cerebral vessels during AOT was noted on the 3d day, rather than on the day of landing. The increased tonus of small arteries and arterioles, which was observed following spaceflights was instrumental in reducing arterial influx to the brain, whereas the tonus of large and medium-sized arteries remained unchanged after spaceflights lasting up to 8 days. This confirms once more the view we previously expounded that small arteries and arterioles play the part of the main actuating element in regulating cerebral blood flow. Evidently, the constrictive reactions of small arteries and arterioles during and after spaceflights prevent plethora of the brain, and this is also aided by constriction of veins and relative increase in venous efflux from the cranial cavity [2, 3, 6]. These reactions to increased influx of blood to the head persist for some time, even after short spaceflights. Thus, on the 14th day after 7-day spaceflights, the AOT showed less pulsed filling of the hemispheres and vertebrobasilar system than preflight. However, it should be noted that high indicators of tonus of arteries, arterioles and veins of the brain were demonstrable after spaceflights with tilts of -15 and -30°, whereas at -45° they demonstrated a drastic decline following spaceflights (see Figures 1 and 2, b and c). This led to significant increase in filling (plethora) of the brain during AOT with a tilt of -45°. While the AOT at tilt angles of -15 and -30° was subjectively perceived as comfortable following a spaceflight, particularly in the first few postflight days, a tilt to -45° elicited complaints of a sensation of blood rushing to the head, sensation of bursting head and fever, pulsation of cervical vessels. Evidently, tilting the trunk to an angle of -45°, which is associated with such excessive delivery of blood to the brain, is an inadequate load to assess resistance of the cerebrovascular system to cranial redistribution of blood, and vascular reactions to such a load could hardly serve as grounds for prognosis of endurance of weightlessness. Perhaps, it would be more expedient for preflight and postflight expert evaluation of cosmonauts involved in short-term spaceflights to use the AOT with tilting of the head end of the table to angles of -15 and -30°, omitting the -45° position. Such a change in the test would not affect its informativeness, but would reduce significantly the risk of possible brain tissue damage, particularly after spaceflights. It is quite probable that -45° antiorthostatic conditions postflight are similar to the critical limit of self-regulation of cerebral blood flow, when even minor fluctuations of perfusion pressure could disrupt adaptation mechanisms [7].

The increase in tonus of large and medium-sized arteries of the lung postflight was indicative of a relative overload on the pulmonary circulation, whereas rapid regression of these changes showed that the observed shifts were functional in nature.

In general, readaptation of vessels in different regions following spaceflights lasting up to 8 days occurred between the 3d and 14th days; the changes were functional and did not require special correction.

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HUMAN VESTIBULAR REACTIONS TO GALVANIC STIMULATION OF LABYRINTHS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 6 Apr 82) pp 48-52

[Article by G. I. Gorgiladze, G. I. Samarin and S. N. Rusanov]

[English abstract from source] The development of illusionary movements and oscillations of the total body mass center in response to labyrinthine stimulation by ascending and descending current was investigated in 37 healthy test subjects. The stimulation of each labyrinth separately or both labyrinths by the current of opposite direction caused illusionary sensations of tilts, turns and tumbles in various planes. When the test subjects were on the stabilographic platform, their total body mass center shifted toward the anode. Simultaneous stimulation of both labyrinths by the current of one direction produced qualitatively new reactions, such as illusionary movement and displacement of the mass center toward the sagittal plane.

[Text] It is known that stimulation of the labyrinths with direct current is associated with typical reactions: nystagmus, changes in posture, illusions of movement and autonomic signs [1-11]. At the same time, electrophysiological studies on animals established that the nature of vestibular afferentation, as well as neuronal reactions in different structures of the central nervous system, is determined by the direction of direct current (cathode, anode), as well as which labyrinth (left or right) is stimulated [12-18].

Our objective here was to study the vestibulomotor (according to fluctuations of general center of gravity [mass] of the body--GSG) and vestibulosensory reactions to stimulation of labyrinths with direct current in ascending and descending directions.

Methods

The studies were conducted on 37 men 18 to 23 years of age. The criteria for screening subjects were: normal hearing and vision, no history of diseases of the ear, vertigo or cerebrocranial trauma. Intensive exercise, intake of alcoholic beverages or hypnotics were not allowed for 2 days prior to the study. The labyrinths were stimulated with direct current using the "Galvanizer" instrument [19]. To deliver current to the labyrinths, we used flat silver chloride

electrodes 10 mm in diameter, which were pressed against the temples, in front of the tragus with spring-loaded clamps. The reference electrode, in the form of a steel plate 40×50 mm in size was secured to the dorsal surface of the neck with a rubber strip. A mixture of alcohol and ether was used to remove oil from the skin under the electrodes, and the skin was additionally swabbed with electrode paste. For better contact, the electrodes were wrapped in gauze saturated with saline. The tests were conducted at electrode resistance not exceeding 5-7 kΩ.

We used the following types of stimulation of labyrinths with direct current: separate stimulation of each labyrinth with the anode and cathode (monaural monopolar galvanization); simultaneous stimulation of both labyrinths with current differing in direction (binaural bipolar galvanization); simultaneous stimulation of both labyrinths with current of the same direction (binaural monopolar or equal galvanization).

We determined the threshold levels of current eliciting illusions of movement in the dark with the eyes closed, in seated and supine position with the head elevated at an angle of 30°. To record fluctuations of the body's GCG the subjects assumed a comfortable stance on the stabilograph platform (feet turned out at 40-45°). We recorded with an ink tracer the fluctuations of GCG in sagittal and frontal directions with fixation of the gaze and in the dark with the eyes closed. In a number of instances, in addition to the stabilogram, we recorded the pneumogram with a carbon sensor. Marks were made on one of the recorder's channels to indicate electric stimulation of the labyrinths. In determining the thresholds of appearance of illusions, galvanization of labyrinths lasted 10 s and for recording GCG fluctuations it lasted 20-60 s. There were 5-min intervals between tests. On the stabilographic tracings, we determined the average frequency of basic GCG oscillations in the frontal direction for 20 s. During monaural monopolar galvanization of the labyrinth with 5 mA current, we assessed the difference between GCG oscillations using conventional formulas, as a percentage of overall reaction:

$$\frac{(a) + (b) - (c) - (d)}{a + b + c + d} \cdot 100\%$$

with anode and cathode stimulation and

$$\frac{(a) + (c) - (b) - (d)}{a + b + c + d} \cdot 100\%$$

when the right and left labyrinths were stimulated with the anode and cathode (asymmetry).

In addition, we estimated the so-called directional overbalance:

$$\frac{(a) + (d) - (b) - (c)}{a + b + c + d} \cdot 100\%$$

where a and b is frequency of the body's GCG oscillations upon stimulation of the left and right labyrinth, respectively, with the anode, c and d is the same for use of cathode, $a + b + c + d$ is frequency of GCG oscillations upon stimulation of right and left labyrinths with anode and cathode (general reaction).

We also used the above formulas to determine the parameters of threshold sensitivity of labyrints according to illusory reactions to monaural monopolar galvanization of labyrinths.

Results and Discussion

Threshold values of direct current that elicited illusory sensations of motion were related to the mode of labyrinth galvanization. They were lower with binaural bipolar stimulation and increased by 1.5-2 times with monaural monopolar galvanization. In seated and supine positions, illusions occurred at virtually the same current. In 24 subjects, there was about 6% difference between threshold sensitivity of labyrinths to the anode and cathode in supine position; asymmetry between the right and left labyrinths and directional overbalance did not exceed 7% (see Table). At the same time, 13 subjects presented more marked difference in all three parameters. In 7 of them, there was 14-19% more sensitivity to the anode and in the other 6 subjects 10-17% more to the cathode. Asymmetry between labyrinths constituted 9-18%, while directional overbalance to the left or right constituted 11-20%. The illusions consisted of sensations of turning, bending, rocking or rotating in different planes. At high current power (8-10 mA) the sensation of ringing in the ears [tinnitus] appeared in some cases.

Threshold levels of direct current, in mA, eliciting illusions with different modes of labyrinth galvanization in health subjects, in supine (top figures) and seated (bottom figures) positions

BINAURAL BIPOLAR GALVANIZ.	MONAURAL MONOPOLAR GALVANIZATION				BINAURAL MONOPOLAR GALVANIZATION	
CATHODE ON RIGHT, ANODE ON LEFT	CATHODE ON		ANODE ON		CATHODE ON BOTH LABYRINTHS	ANODE ON BOTH LABYRINTHS
	RIGHT	LEFT	RIGHT	LEFT		
1,20±0,18 1,30±0,20	1,80±0,31 1,90±0,41	1,90±0,25 1,71±0,30	2,30±0,33 2,18±0,53	2,05±0,29 2,26±0,39	6,91±1,10 6,53±1,41	5,75±0,82 5,78±1,12

In addition to illusion of movement, galvanization of labyrinths elicited impairment of stability of erect position (changes in GCG oscillations; Figures 1-3). With binaural bipolar stimulation of the labyrinths, the first changes in GCG oscillations were noted at 0.7-1.0 mA. With further increase in power, the oscillations became more distinct. Their amplitude and frequency increased. With mild stimulation, the oscillations of the body's GCG occurred primarily in the frontal plane; with increase in power, body movements in the sagittal plane appeared and became more noticeable (see Figure 1). In most cases there was more or less prolonged deflection of the body in some direction, against the background of which there were rapid oscillations of GCG. With monaural monopolar stimulation of the labyrinths, the first changes in fluctuation of GCG appeared at 1.5-2 mA. With both bipolar binaural and monaural monopolar stimulation of the labyrinths, the direction of shift of GCG usually

depended on the direction of the current: GCG always shifted to the anode (see Figure 2). At high power, there was a drop in the same direction. Background frequency of basic oscillations of GCG in a frontal direction constituted a mean of 17.1±3.2/min. With monaural monopolar galvanization of the right and left labyrinths with 5 mA current, the frequency of GCG oscillations increased by 1.3-1.8 times. In most subjects, the difference in oscillations of GCG under the influence of descending or ascending current did not exceed 5%; asymmetry between labyrinths constituted about 7% and directional overbalance, 8%. At the same time, subjects with different threshold sensitivity for onset of illusions presented a difference in reactions to anode and cathode upon stimulation of the right and left labyrinths, as well as directional overbalance that reached 13, 19 and 24%, respectively.

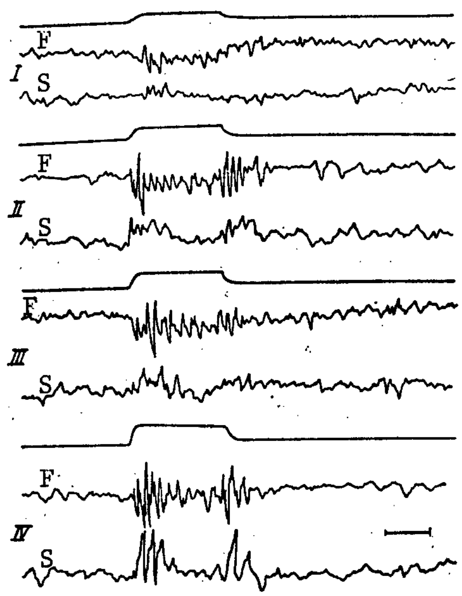

Figure 1.
Effect of labyrinth stimulation with direct current differing in power on GCG oscillations (cathode on the right, anode on the left). Time scale 10 s

I-IV) tracings with current of 1, 2, 3 and 4 mA, respectively, with the subject in the dark and eyes closed.

Here and in Figure 2:
top tracings--stimulation mark
F) frontal stabilogram
S) sagittal stabilogram

When direct current of the same direction was passed through both labyrinths (binaural monopolar galvanization), there were qualitatively different illusions of movement and changes in GCG oscillations. First of all, it was determined that illusions of movement with this mode of stimulation of labyrinths appeared at considerably stronger current, averaging about 6-7 mA (see Table). When the cathode was delivered to both labyrinths there were illusions of the body tilting forward and, with the anode, backward. These sensations of deflection of the body usually coincided with the direction of GCG shift on stabilographic tracings (see Figure 2). The earliest changes in GCG were noted at 4-5 mA or more. In some subjects, illusions did not occur, even at 10 mA (in 9 and 7 in supine position, and in 7 and 8 in seated position, with ascending and descending directions, respectively). It must be emphasized that the threshold current eliciting illusions and changes in GCG oscillations, as well as their nature, were virtually the same as with separate stimulation of each labyrinth in subjects with more or less marked right- and left-sided asymmetry under conditions of equal galvanization of both labyrinths.

In the case of relatively prolonged galvanization of labyrinths, the changes in GCG oscillations were more noticeable immediately after delivery of current and they subsequently regressed gradually, in spite of unchanged stimulation (see Figure 3). They were usually more significant in the dark than with fixation of gaze (see Figures 2 and 3). Galvanization of the labyrinths could lead to change in external respiratory rate; however, this had virtually no effect on the stabilographic tracings (see Figure 2).

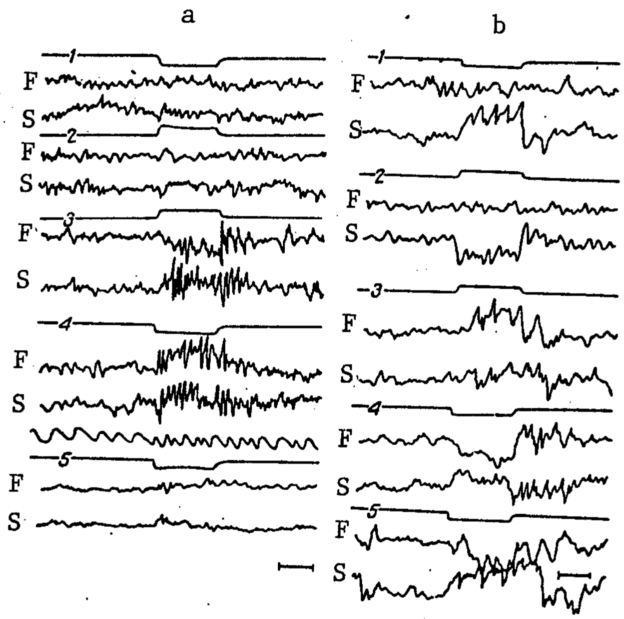

Figure 2. Effect of different modes of labyrinth galvanization on GCG oscillations in two subjects (a and b)

a) stabilograms with delivery through both labyrinths of ascending (1) and descending (2) current; with anode on the left and cathode on the right (3); anode on the right, cathode on the left with the subject's eyes closed (4) and fixed gaze (5)

b) stabilograms with delivery through both labyrints of ascending (1) and descending (2) current; anode on the right and cathode on reference electrode (3); cathode on the right, anode on reference electrode (4); anode on the left, cathode on the right (5)

Bottom tracing in a (5)--pneumogram. Upward deflection of frontal stabilograms corresponds to right shift of GCG, downward deflection shows body shift to the left; upward deflection of sagittal stabilograms corresponds to body shift forward and deflection down, to body shift backward. Stimulating current 5 mA in a and 6 mA in b. Time scale 10 s.

Thus, it was established that delivery of direct current through the labyrinths of healthy subjects is associated with very definite subjective and objective reactions in the form of illusions of motion and oscillations of body GCG. The nature of these changes was determined by the direction of stimulating current and side that was stimulated. Seeming motion, as well as shift of GCG, were usually in the direction of the anode. In this regard, it is opportune to recall the results of previous studies on animals, according to which application of the anode to the labyrinth led to inhibition of background impulsation of the vast majority of neurons of vestibular nuclei, vestibular projection and sensorimotor zone of the cerebral cortex on the stimulated side [13-18]. When direction current of different directions was delivered to both labyrinths, the thresholds for onset of illusions of movement, as well as GCG shifts, were considerably lower than with separate stimulation of each labyrinth with the

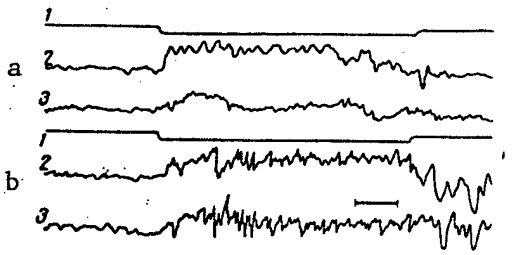

Figure 3.
Changes in GCG oscillations during prolonged galvanization of labyrinths with gaze fixation (a) and in the dark with the subjects' eyes closed (b). Time scale 10 s
1) stimulation (cathode on the left, anode on the right, 5 mA)
2, 3) frontal and sagittal stabilograms, respectively

same current in both ascending and descending directions. Apparently, this is attributable to the fact that, with this mode of labyrinth stimulation, there is considerably greater imbalance in activity of vestibular nuclei bilaterally than with stimulation of one labyrinth [13-16].

In most subjects, illusions of movement appeared at virtually the same levels of stimulating current regardless of its direction or side stimulated. The same was observed with regard to changes in oscillations of GCG in standard galvanic tests. At the same time, some subjects presented more or less marked asymmetry of tested reactions and directional overbalance with stimulation of labyrinths using direct current of different directions. We know that overt asymmetry of vestibular reactions, particularly caloric nystagmus, is seen in healthy subjects under stress and in individuals suffering from vegetovascular dystonia [20-21].

Qualitatively different reactions were demonstrated in response to symmetrical equal stimulation of both labyrinths, which was induced by delivery through both labyrinths of direct current of the same direction. First of all, most subjects developed illusory sensations, as well as shifts of body GCG, with such stimulation of the labyrinths only when power of stimulating current was significantly raised. Another distinction was referable to the nature of the reactions: seeming movements and shifts of GCG occurred mainly in the sagittal plane. Apparently, this phenomenon can be explained in the following manner. In studies of functional organization of vestibular nuclei in animals, it was found that there are at least two systems of communication between nuclear neurons and both labyrinths. The neurons of one system reacted reciprocally to separate stimulation of the right and left labyrinth with direct current of the same direction, whereas such reciprocity was lacking in neurons of the other system and they reacted in the same way to stimulation of both labyrinths [14-16]. On the basis of these data, it can be assumed that, with equal stimulation of both labyrinths, afferentation from reciprocally organized paired elements of the labyrinths is blocked in vestibular nuclei on both sides due to mutually reciprocal inhibition. At the same time, reactions were demonstrated that are related to synergistically organized paired elements of the labyrinths. Moreover, with delivery of descending direct current through both labyrinths there should be bilateral inhibition of vestibular function. The high thresholds for onset of reactions to equal galvanization of both labyrinths could be related to distinctions referable to both transformation of vestibular afferentation in vestibular nuclei proper and organization of vestibulospinal connections.

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HUMAN BLOOD BIOGENIC AMINES AND THEIR PRECURSORS IN ANTIORTHOSTATIC POSITION AND WITH INTAKE OF PHARMACOLOGICAL AGENTS FOR PREVENTION OF SEASICKNESS SYNDROME

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 1 Mar 82) pp 53-56

[Article by N. A. Davydova, S. L. Il'ina and V. V. Sabayev]

[English abstract from source] The 6-hour exposure to head-down tilt at -15° was accompanied by an increased blood content of adrenaline and noradrenaline, thus indicating the activation of the sympathoadrenal system. The catecholamine concentration was shown to be proportional to the head-down tilt time. The exposure also led to an increase of the content of serotonin and left the content of 5-hydroxytryptophan, tryptophan, histamine and histidine unchanged. After administration of ephedrine and especially, ephedrine in combination with pipolphen the increase in the concentration of catecholamines and serotonin became significantly less pronounced.

[Text] Biogenic amines play an important part in preserving homeostasis and development of adaptive reactions in the body in the presence of extreme factors. Much significance is attributed to their levels with reference to pathogenesis of the seasickness syndrome and mechanism of preventive effects of pharmacological agents [1-5].

It is generally believed that immersion, antiorthostatic hypokinesia for different periods of time and brief antiorthostatic position (AP) or AP with different tilt angles [6, 7] are the most adequate methods of simulating body reactions inherent in the early period of adaptation to weightlessness.

In this article, we submit the results of a study of the effect of brief AP on levels of biogenic amines and their precursors--epinephrine (E), norepinephrine (NE), serotonin (S), tryptophan, 5-hydroxytryptophan, histamine (Hm) and histidine (Hd)--in human blood and with use under these conditions of pharmacological agents against the seasickness syndrome.

Methods

These studies were conducted with 10 healthy male subjects 25-45 years of age, who were put under clinical conditions for 4 days 1 day before the study (2 subjects at a time). On the following day background clinicophysiological and biochemical tests were made (first background period), and they were repeated on the 3d day at the hospital 1 h before moving the subjects to AP at a tilt angle of -15° for 6 h (second background period). We took samples of venous blood in the 1st and 2d background periods, at the end of the 3d and 6th h in AP, 30 min after returning the subjects to horizontal position and the following morning.

Pharmacological agents--ephedrine (0.025), ephedrine (0.025) + scopolamine (0.0006), ephedrine (0.025) + pipolphen (0.025)--were given to the subjects in capsules 30 min after placing them in AP. Since the results of the series where placebo (lactose in a dosage of 0.25) was used did not differ from the control series of studies (AP without pharmacological agents), we deemed it justified to combine them in a single control group. Thus, there were 10 people in the control group and 5 in each of the others.

Catecholamine (CA), E, NE, as well as S, Hm and their precursors were assayed fluorimetrically [8-10]. The obtained data were processed by the method of variation statistics using the criterion of Student-Fisher.

Results and Discussion

The results of tests made 1 day before placing the subjects in AP (first background period) were indicative of normal E and NE levels in blood (Table 1). Statistical means constituted 0.82±0.06 and 1.00±0.11 μg/ℓ, respectively. Just prior to AP (2d background period) there was a reliable increase in concentration of both E and NE (1.47±0.12 and 1.44±0.15 μg/ℓ, respectively) in all series of studies. The E/NE ratio showed virtually no change. Analogous results had been obtained previously in studies using an immersion medium [11-13]. The increase in activity of the hormonal part of the adrenosympathetic system (ASS) under these conditions can apparently be attributed to development of emotional stress reaction prior to AP.

In the control tests, CA content of blood increased drastically in AP, and remained high even 30 min after changing the subjects to horizontal position. The elevated NE level persisted on the next day [or days]. It should be noted that the concentrations of E and NE depended directly on duration of AP (see Table 1). Thus, at the end of the 3d h of AP CA concentration increased by 2.5-2.8 times, as compared to the 1st background period and after 6 h it increased by 4.1 times. It can be assumed that the high CA content in AP was related to both nervous-emotional stress and compensatory reaction of the ASS responsible for maintaining homeostasis against the background of redistribution of body fluids to the upper half of the body. As shown by N. A. Davydova et al. [14], elevation of CA level in blood and urine during immersion occurs against the background of hypometabolism of CA and is attributable to their discharge from the reservoir.

Table 1. CA level in human blood (μg/ℓ) in AP with and without intake of pharmacological agents to prevent seasickness syndrome (M±m)

AGENT	BACKGROUND PERIOD		AP		RECOVERY PERIOD	
	1	2	3 H	6 H	30 MIN	1 DAY
	EPINEPHRINE					
CONTROL	0,74±0,06	1,30±0,08*	2,33±0,11*	3,33±0,13*	2,05±0,22*	0,98±0,10
EPHEDRINE	0,75±0,06	1,53±0,11*	1,80±00,7***	2,20±0,14***	1,63±0,11*	1,28±0,24
EPHEDRINE+SCOPOLAMINE	0,98±0,09	1,62±0,18*	2,54±0,18*	2,91±0,15***	1,77±0,19*	0,94±0,08
EPHEDRINE + PIPOLPHEN	0,82±0,05	1,43±0,12*	2,07±0,21*	2,28±0,11***	1,63±0,11*	0,70±0,07**
	NOREPINEPHRINE					
CONTROL	0,91±0,10	1,36±0,15*	2,48±0,19*	4,10±0,42*	2,46±0,19*	1,47±0,13*
EPHEDRINE	1,06±0,15	1,59±0,18*	1,87±0,11***	2,30±0,14***	1,59±0,14***	1,27±0,10
EPHEDRINE + SCOPOLAMINE	1,12±0,11	1,50±0,13*	2,70±0,23*	2,74±0,24***	2,16±0,16*	1,03±0,14**
EPHEDRINE + PIPOLPHEN	0,94±0,08	1,32±0,15*	1,01±0,26**	1,08±0,25**	1,07±0,11**	0,92±0,10**

Here and in Table 2:
*Reliability of differences with $P<0.05$ in relation to 1st background period.
**Same in relation to period of control studies.

Table 2. Levels of S and its precursors in human blood (μmol/ℓ) in AP with and without intake of pharmacological agents to prevent seasickness syndrome (M±m)

AGENT	BACKGROUND PERIOD		AP		RECOVERY PERIOD	
	1	2	3 H	6H	30 MIN	1 DAY
	SEROTONIN					
CONTROL	0,50±0,02	0,79±0,08*	1,17±0,08*	1,45±0,12*	1,39±0,11*	0,85±0,03*
EPHEDRINE	0,56±0,02	0,68±0,04*	0,94±0,06***	1,26±0,10*	1,11±0,11*	0,87±0,08*
EPHEDRINE + SCOPOLAMINE	0,66±0,04	0,83±0,05*	1,30±0,20*	1,73±0,14*	1,50±0,09*	1,08±0,08***
EPHEDRINE + PIPOLPHEN	0,50±0,04	0,68±0,05*	0,67±0,08**	1,33±0,16*	0,78±0,13**	0,68±0,06**
	5-HYDROXYTRYPTOPHAN					
CONTROL	0,14±0,01	0,14±0,01	0,15±0,01	0,15±0,02	0,16±0,03	0,15±0,02
EPHEDRINE	0,16±0,01	0,15±0,02	0,15±0,01	0,14±0,02	0,13±0,02	0,14±0,01
EPHEDRINE + SCOPOLAMINE	0,18±0,01	0,17±0,01	0,17±0,01	0,16±0,01	0,16±0,01	0,16±0,07
EPHEDRINE + PIPOLPHEN	0,15±0,01	0,14±0,01	0,14±0,02	0,14±0,02	0,14±0,02	0,14±0,01
	TRYPTOPHAN					
CONTROL	46,9±0,5	47,0±0,9	47,3±1,7	46,8±1,1	46,5±0,8	46,2±0,8
EPHEDRINE	48,7±6,6	49,1±3,9	50,7±4,4	46,6±4,1	44,7±4,1	42,2±4,4
EPHEDRINE + SCOPOLAMINE	48,3±6,2	50,6±6,9	52,4±10,9	45,9±7,3	39,7±3,4	45,8±9,2
EPHEDRINE + PIPOLPHEN	48,0±2,6	48,4±2,4	50,0±3,0	46,4±2,5	48,7±1,7	49,2±0,5

The pharmacological agents did not prevent the heightened ASS reaction to AP, but blood CA with intake thereof was usually lower than the level in the control studies (see Table 1). In this respect, ephedrine and ephedrine combined with pipolphen were the most effective. With intake of these agents, E concentration in blood rose by 2.2 and 2.5 times, respectively at the end of the 3d h in AP (versus 2.8-fold increase in the control), by 2.7 and 2.8 times at the end of the 6th h (versus 4.1-fold).

The above agents had an analogous effect on NE content. Intake of ephedrine raised its level by 1.9 and 2.3 times after 3 and 6 h, respectively, in AP, whereas control levels were 2.5 and 4.1 times higher than the background at the same times. It should be noted that, with the combined use of ephedrine with pipolphen, blood NE level showed virtually no difference from background values throughout the period in AP. This can be attributed to synergism in action of ephedrine and pipolphen on NE metabolism in AP, since ephedrine alone elicited only a partial normalizing effect. The results are indicative of the possibility of arresting the stress reaction that develops during the period of adaptation to extreme factors by using optimum combinations of tranquilizers (in reduced dosage) with adrenomimetics, in particular ephedrine, since it is known that stress reactions are characterized primarily by increased discharge of expressly NE, rather than E.

Table 2 lists data on the effect of AP and pharmacological agents on levels of S and its precursors in blood. The results of the studies conducted in the 2d background period indicate that there was a 30% increase, as the average for different groups ($P<0.05$), in blood S concentration 1 h before changing the subjects to AP. This change can be attributed to nervous-emotional stress, since comparable results had been obtained by several authors in the presence of emotional stress, in particular, while waiting for exposure to accelerations on a centrifuge [15].

In the control series of studies, an even greater elevation of S level in AP was demonstrated. Thus, 3-h in AP increased S concentration by 2.1 times and 6-h AP by 2.6 times. An elevated S level was also observed in the recovery period: 2.5-fold after 30 min and 1.5-fold on the next day.

After intake of ephedrine, there was less marked increase in blood S concentration in AP. E hedrine combined with pipolphen normalized completely the S content at the end of the 3d h of AP and in the aftereffect period, which can also be attributed to arrest of nervous-emotional stress by pipolphen. After intake of ephedrine combined with scopolamine, blood S level was somewhat higher at all tested times ($P>0.05$) than in the control series of tests.

We failed to demonstrate significant changes in 5-hydroxytryptophan and tryptophan levels in blood in the background period, AP and recovery period. This could be an indirect indication of the fact that the increase in S level under antiorthostatic conditions is attributable to its discharge from its reservoir and change in function of inactivating systems.

Unlike CA and S, the levels of Hm and its precursor Hd did not undergo deviation from normal values in AP, in either the control studies or series with intake of pharmacological agents.

Thus, the results of these studies indicate that the changes due to AP are associated with hormonal changes in the ASS, in particular an increase in CA content. There is also an increase in S content. Activation of the ASS can be viewed as an adaptive reaction to antiorthostatic position, which is related to maintenance of hemodynamic homeostasis. The data obtained in the series of studies using pharmacological agents indicate that it is possible, in principle, to use drugs to correct metabolic changes in CA and S at the early stage of adaptation to antiorthostatic position and weightlessness. These findings must be taken into consideration in interpreting both the hemodynamic changes that occur in AP and the mechanisms of effects of drugs to prevent the seasickness syndrome.

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RESULTS OF QUANTITATIVE CYTOLOGICAL ANALYSIS OF RAT THYMUS AFTER FLIGHTS IN BIOSATELLITES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 30 Sep 81) pp 56-61

[Article by F. V. Sushkov,* S. V. Rudneva, G. N. Durnova and T. F. Ponomareva]

[English abstract from source] The mitotic activity, destruction and volume of thymocytes were investigated on histological preparations of the thymus of rats flown onboard Cosmos-782 and Cosmos-936. The cytological data showed that immediately after touchdown large quantities of thymocytes of the cortical matter perished. The mitotic activity of the remaining undamaged thymocytes declined and returned to normal 9 hours after recovery. The rats that were centrifuged inflight (at 1 g) did not display a lower mitotic activity or noticeable destruction of thymocytes. Karyometric measurements demonstrated that the population of thymic lymphocytes was heterogeneous in the nuclear volume: it consisted of three peak classes of nuclear volumes. The variance curves of nuclear volumes of lymphocytes of the medullary matter were drastically shifted toward large numbers. An increase in the nuclei of thymocytes of the cortical matter in the flight rats was stable and persisted till R+25.

[Text] Rats develop accidental involution of lymphoid organs after long-term flights in biosatellites in weightlessness [1, 2]. There is reduction of thymus mass and destruction of thymocytes in the cortex. These changes are reversible, and there is complete restoration of structural organization of the thymus 25 days after returning to earth. In order to assess the complex phenomena that occur in the thymus of rats flown in biosatellites, it is necessary to have quantitative data about the intensity of proliferation and destruction of thymocytes, as well as information about their cytophysiological activity. Only the weight [mass] of the organ was measured in the cited works.

We submit here the results of determination of mitotic activity (MA), extent of thymocyte destruction and results of karyometry as parameters of functional activity of cells [3].

*This article is one of the last works by the late Fedor Vasil'yevich Sushkov, candidate of biological sciences, participant of the Great Patriot War, member of the CPSU, who was an outstanding Soviet cytologist. For the last 17 years of his life, F. V. Sushkov was concerned with problems of space cytophysiology, and his research made a substantial contribution to current views on the effect of weightlessness and other extreme factors on living cells.

Methods

Histological preparations* of the thymus from male Wistar SPF rats, who were flown in Cosmos-782 and Cosmos-936 biosatellites for 19.5-18.5 days, served as the material for our study. Rat that had been in weightlessness during the spaceflight were decapitated 4.5-9 h (W_1 group), 9-12 h (W_2 group) and 25 days (W_3 group) after returning to earth. Animals flown aboard Cosmos-936 with artificial gravity (AG), which was created by rotation on a centrifuge (1 G acceleration) were sacrificed 4.5-9 h (C_1 group) and 25 days (C_2 group) after landing. The thymus from rats used in ground-based model experiments, in which all spaceflight conditions were simulated, with the exception of weightlessness (M_1, M_2 and M_3 groups) and rats kept in the vivarium (V_1, V_2 and V_3 groups), which were decapitated at the same postexperiment times as the flight groups of animals, served as controls. Thymocyte MA was assessed by the mitotic index (MI), which was expressed as the number of mitoses per field of vision and per thousand. We counted at least 100 fields of vision for the cortex of the thymus of each rat. To express MI per thousand, we determined the number of structurally unchanged cells in a space circumscribed by a special grid 2500 μm in size, and then scaled it to the entire visual field; we counted a total of at least 25,000 cells. We determined the number of degenerated elements, considering a cell to be "dead" when detritus fragments were at least one-third the diameter of a lymphocyte and the nucleus was distinctly pyknotic.

We measured the volume of cell nuclei using a modification of the method in [4], drawing the outlines of nuclei of lymphocytes from different parts of the cortex and medulla, for at least 100 nuclei from each zone, using an RA-6 drafting [drawing] machine. We drew the nuclei of cortical cells situated at least 1000 μm away from the connective tissue capsule; we also determined MA in the same cortical regions. In all, we examined 65 rats.

Results and Discussion

The results of cytological analysis of the thymus of rats flown in Cosmos-782 biosatellite are listed in Table 1. In the flight group of rats sacrificed 9-12 h after landing, the cortex of the thymus revealed many destroyed cells, which were virtually absent in control animals and rats exposed to dynamic factors in the ground-based model experiment. There was a corresponding decrease in number of cells per unit area. MI in the cortex of the thymus of flight group rats scaled to a visual field was 20% lower than in the control and ground-based model experiment ($0.05<P<0.1$). However, when MI was expressed per thousand, we failed to demonstrate any depression of MA in the flight group of rats.**

The presence of morphological evidence of acute stress, in the form of destruction of thymocytes in experimental animals decapitated 9-12 h after landing, warrants the belief that depression of thymocyte MA occurs at earlier or later postflight

*Method used to make preparations was described previously [2].

**These data indicate that the method of calculating MI per visual field may yield erroneous information about MA in cases where there is cellular destruction.

times. The results of studying thymocyte MA in rats flown in Cosmos-936, which were sacrificed at earlier postflight times than those flown in Cosmos-782 confirmed this. As can be seen from the data listed in Table 2, there was a reliable decrease in MI in 3 rats of the flight group, which were decapitated within the first 7 h (W_1 group). In the remaining animals of the W_1 group, as in rats in the W_2 group, which were decapitated 9-12 h after the biosatellite landed, thymocyte MA did not differ from that of control groups of rats. Just as rapid recovery of thymus MA has been described in rats after giving them cortisone [5].

Table 1. MI and extent of destruction of thymus cells in rats used in experiment aboard Cosmos-782 biosatellite

ANIMAL GROUP	NUMBER OF ANIMALS	CELLS/FIELD ($S = 0.02\ MM^2$)	CELLS WITH PYKNOTIC NUCLEI, %	MI	
				PER FIELD	PER THOUSAND
W_2	6	283±6,0 $P<0,001$	17,8±1,39 $P<0,001$	4,1±0,26 $0,05<P<0,1$	13,9±0,58 $P>0,5$
M_2	5	370±5,9	0,5±0,08	5,2±0,43	14,2±1,16
V_2	5	373±4,9	0,3±0,06	5,0±0,39	13,3±0,84
W_3	4	—	—	5,3±0,31 $P>0,5$	14,8±0,87 $P>0,1$
M_3	6	—	—	6,2±0,46	17,2±0,90
V_3	6	—	—	6,0±0,43	16,6±1,18

Table 2. MI and extent of thymocyte destruction in rats flown in Cosmos-936

ANIMAL GROUP	NUMBER OF ANIMALS	CELLS/FIELD ($S = 0.02\ MM^2$)	CELLS WITH PYKNOTIC NUCLEI %	MI	
				PER FIELD	PER THOUSAND
W_1	3	300±6,0 $P<0,001$	18,5±1,2 $P<0,001$	4,5±0,48 $P<0,05$	13,1±1,26 $P<0,05$
C_1	4	390±6,0	0,9	6,9±0,34	17,9±0,46
M_1	4	385±8,6	0,4	6,9±0,42	17,7±1,24
V_1	4	398±7,8	0,2	6,1±0,39	17,0±1,09
W_2	4	330±8,0 $P<0,005$	17,5±1,9 $P<0,001$	5,2±0,43 $0,05<P<0,1$	15,8±0,43 $P>0,5$
M_2	4	379±7,3	0,5	6,2±0,32	16,6±1,09
V_2	4	390±7,1	0,2	6,8±0,58	17,5±1,20

The tested parameters of the thymus of flight groups of rats did not differ from the corresponding control values 25 days after landing, i.e., there was restoration of structure of this organ. In rats flown under artificial gravity, there was no decline of MI or appreciable cellular destruction (see Table 2). Thus, in this group of animals we failed to demonstrate signs of a stress reaction. This warrants the conclusion that the changes in the thymus of W_1 group rats are the consequence of stress, which developed with the change from weightlessness to earth's gravity. Such secondary stress has been described in the first few hours of the recovery period in rats submitted to prolonged hypokinesia [6].

The quantitative data confirmed the results of histological studies of the thymus [1, 2, 7] and demonstrated that there is massive destruction of thymocytes in the cortex of rats within the first few hours after landing following an 18.5-19.5 day exposure to weightlessness. The MA of cells that remained intact was diminished. Depression of MA was brief and, already 9 h after landing, reproductive capacity of the thymocytes was virtually restored to the initial level.

Results of karyometry. It is possible to classify lymphocytes according to size by means of morphometry [8, 9]. Melik-Gaykazyan et al., who used as a criterion the coefficients of expression and asymmetry, analyzed the variational curves of diameters of cells and nuclei of lymphocytes in peripheral blood and lymphoid organs. They were trying to demonstrate the heterogeneity of bone marrow lymphocyte population [10] in this manner.

Measurement of nuclei of all lymphocytes encountered from the cortex to the medulla yielded multipeak variational curves. This is indicative of phenotypic heterogeneity of the thymocyte population for this character. Separate measurement of lymphocyte nuclei revealed that, in all control and experimental rats, the medullary cell nuclei were considerably larger than those of cortical lymphocytes. The variational curves of nucleus sizes in different zones of the thymus of all animals distinctly demonstrated three peak classes of nuclei, the values of which corresponded to 1.6, 1.7 and 1.8 log or 40, 50.2 and 63.1 μm^3. It appears that these classes correspond to small, medium-sized and large lymphocytes. However, a comparison of these data to the results of other morphometric studies of the rat thymus revealed [8, 9] that such interpretation of experimental data is not sufficiently argumented. The demonstrated peak classes of nuclear volumes most likely correspond to small and medium lymphocytes. Apparently, this is consistent with the real state of the lymphoid population, since it is known that there are considerably fewer large lymphocytes than small and medium ones. On the illustrated variational curves, the cells to the right of the 1.9 log class could be labeled as large lymphocytes. With such division of thymocytes according to volume of their nucleus, we find that, in control animals, the share of large lymphocytes is 10-15% of the cell population. A total of 70-80% of the cells conform to the above-described peak classes and 10-15% are referable to classes that constitute 1.5-1.4 log. The presence of three peaks on the variational curve apparently reflects the difference between functional state of cells that are classified by histologists as small and medium-sized lymphocytes.

It is justified to compare our experimental data to the morphometric results of other researchers [8, 9], since we used sections of the same thickness and with the same fixation. The rather large thymocyte diameters listed in Table 3 are apparently attributable to the fact that the authors worked with impression preparations; they did not describe the fixing method [10].

The differences between geometric means of lymphocyte nuclear volumes in the cortex of control rats and animals used in the model experiment did not exceed 15%, and they are wihtin the statistically permissible range, which enables us to work with weighted means and overall variational curves. In the medulla, the fluctuations of mean volumes of nuclei reached a statistically significant level in isolated instances (±25%).

In table 3, the animals are distributed according to peak class of nuclear volume in cortical and medullary thymocytes. As we see, there is prevalence in experimental groups of animals in the medulla of which the peak class of thymocyte nuclear volume has a value of 1.8 log. In the W_1 group, all of the animals are referable to this class; in other groups there are rats with the 1.7 log class, but 25 days after the flight the distribution of animals according to this feature differs from the control. In the rat group flown in the biosatellite under artificial gravity, the proportion of animals referable to different peak classes of volumes of nuclei showed virtually no difference from the control.

Table 3. Distribution of thymocytes according to variational series classes in rats flown in Cosmos-936

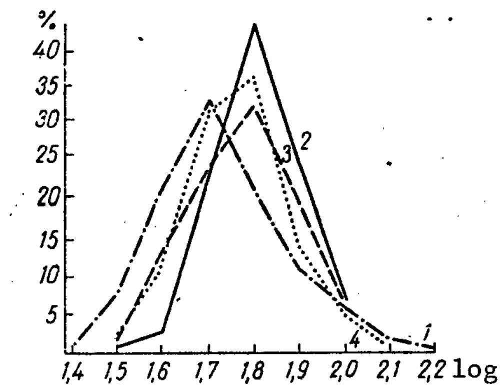
ANIMAL GROUP	THYMUS ZONE	PERCENTAGE OF NUCLEI IN VARIATION SERIES CLASSES				
		1,5 lg AND LESS	1,6lg	1,7lg	1,8lg	1,9lg AND MORE
$V_{1,2,3}+M_{1,2,3}$ ($n=16$, $n_1=1700$)	CORTEX	20,0±2,25	40,0±1,36	24,3±3,65	9,6±0,96	6,1±1,39
W_1 ($n=4$, $n_1=400$)		25,0±2,79	43,0±3,92	24,0±3,92	6,5±0,86	1,5±0,38 $P<0,005$
W_2 ($n=5$, $n_1=519$)		31,0±3,24	39,5±3,14	17,0±3,19	8,0±2,68	4,5±1,48
W_3 ($n=5$, $n_1=502$)		23,0±3,54	38,5±3,65	22,5±4,51	10,0±0,86	6,0±1,93
$V_{1,2,3}+M_{1,2,3}$ ($n=16$, $n_1=1700$)	MEDULLA	8,9±1,07	21,4±2,79	33,6±3,65	21,5±2,04	14,6±2,83
W_1 ($n=4$, $n_1=400$)		1,0±0,56 $P<0,001$	3,5±0,86 $P<0,001$	22,0±3,08 $0,02<P>0,05$	43,0±2,52 $P<0,001$	30,0±4,20 $P<0,01$
W_2 ($n=5$, $n_1=518$)		1,5±0,43 $P<0,001$	13,0±1,07 $P<0,05$	23,5±3,51 $P>0,05$	32,0±3,15 $P<0,05$	30,0±3,51 $P<0,05$
W_3 ($n=5$, $n_1=500$)		2,0±1,29 $P<0,001$	12,5±3,43 $0,05<P<0,1$	30,5±3,65 $P>0,1$	35,5±3,43 $P<0,005$	19,5±2,79 $P>0,05$
C_1 ($n=3$, $n_1=300$)		4,0±1,31 $0,05>P>0,025$	21,0±1,96 $P>0,5$	44,0±3,53 $P>0,05$	23,0±2,54 $P>0,1$	8,0±0,88 $P>0,1$
C_2 ($n=5$, $n_1=500$)		3,5±1,29 $P<0,05$	12,5±1,96 $0,05>P>0,025$	33,5±1,83 $P>0,1$	30,5±3,69 $P>0,05$	20,0±2,83 $P>0,1$

Note: n is the number of animals and n_1 the number of nuclei measured.

In the cortex there is prevalence of cells with peak class of 1.6 log for volume of nuclei. Only 21% of the control animals and rats in the model experiment had lymphocytes in peak class of 1.7 log. The absence of such animals in experimental groups had virtually no effect on the geometric means of nuclear volumes and distribution of nuclei in variational series classes (see Table 3). Table 3 shows that a statistically significant decrease in number of cells in the classes of nuclear volumes of 1.9 log or more was present in the cortex of the thymus only in the W_1 group.

In experimental animals there was drastic shift of the nuclear volume curves for medullary lymphocytes in the direction of higher numbers (see Figure). The variational curves for thymocyte nuclear volumes in model experiments did not differ from those for the vivarium control rats. We failed to demonstrate appreciable enlargement of lymphocyte nuclear volumes in the thymus medulla of animals flown in space while exposed to artificial gravity. The slight shift of the overall variational curve in the direction of higher numbers and increase

to 50% in number of animals in the W group with peak class of 1.8 log, versus 32% in the control, do not exceed the statistically permissible values (see Table 3).



Variational curves of cortical lymphocyte nuclear volumes in thymus of rats flown in Cosmos-936
1) overall control
2-4) W_1, W_2 and W_3 rats flown in Cosmos-936 biosatellite

Thus, enlargement of lymphocyte nuclei in the medulla of the thymus is a consequence of spaceflight factors. Immediately after the flight, there was more marked enlargement of nuceli due to summation of the "flight effect" and the effect of earth's gravity. On this basis, the demonstrated enlargement of nuclei can be referred to cytophysiological symptoms of a stress reaction. Such an interpretation would also be valid for the previously described enlargement of nuclei in the reproductive layers of epithelial cells in the cornea of the same rats. What prevents us from using such an interpretation for the demonstrated phenomenon is its persistence and absence of information in the available literature concerning change in size of cell nuclei in renewable tissues in the presence of stress factors. For this reason, our view is still only a hypothesis, and it requires experimental verification.

According to existing data, it would be more realistic to relate the "swelling" of thymocyte nuclei, which was found in flight groups of animals, to intensification of repair processes in the thymus elicited by stressor-induced destruction of thymocyte mass. However, even with this interpretation, it is difficult to explain why, according to karyometric data, the medulla makes the main contribution to recovery of this organ's structure. Nor should one overlook the fact that, in the thymus, cells of the lymphoid population migrate constantly.

The results of these quantitative cytological studies indicate that changes development in the rat thymus after returning from a spaceflight, which are attributable to the combined effect of two factors: prolonged weightlessness and subsequent return to earth's gravity. In this respect, we concur with conclusions that were drawn on the basis of morphological evaluation of lymphoid organs [2, 7]. At later postflight stages, against a background of morphophysiological "well-being," with respect to normalization of the thymus, signs persisted of an increased functional load on lymphoid tissue of this organ. This is indicated by retention of statistically significant differences in volume of medullary thymocyte nuclei in many experimental animals, as compared to the control.

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INVESTIGATION OF MORPHOLOGICAL AND FUNCTIONAL PROPERTIES OF RAT PERIPHERAL BLOOD AND BONE MARROW CELLS AFTER FLIGHT IN COSMOS-936 BIOSATELLITE

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[Article by G. I. Kozinets, V. I. Korol'kov, I. I. Britvan, I. A. Bykova, N. Ye. Spitsyna, N. N. Talelenova, V. A. Kondrat'yeva and N. A. Chel'naya]

[English abstract from source] Morphofunctional properties of peripheral blood cells of Cosmos-936 rats were examined, using morphological, interferometric and electron microscopic techniques. As follows from the morphological data, immediately after recovery the weightless rats showed symptoms of a stress reaction which disappeared by R+3. The centrifuged rats exhibited less expressed symptoms of this sort. The percentage of bone marrow cell distribution was shifted towards enhanced myelopoiesis and diminished erythropoiesis. By the end of the readaptation period the ratio of bone marrow cell composition returned to normal. Interferometric and electron microscopic examinations did not reveal any irreversible changes in the structure and function of cells that may be caused by zero-g.

[Text] Studies of cosmonauts following spaceflights revealed that there was a reliable decrease in circulating blood mass due to reduction of both plasma and erythrocyte mass volume. The decrease in mass of circulating erythrocytes is based on depression of erythropoiesis [1, 2]. P. A. Korzhuyev [3] mentioned the possibility of depression of erythropoietic activity in bone marrow of cosmonauts [3], and he advanced the thesis that the change from earth's gravity to prolonged weightlessness could disrupt normal activity of the skeleton as a hemopoietic system.

Data obtained from examining rats flown in Cosmos-605 and Cosmos-782 biosatellites are indicative of depression of erythroid elements of bone marrow [4], shortening of erythrocyte life span and increase in spontaneous hemolysis [5].

These circumstances served as grounds for a deeper investigation of morphological and functional properties of peripheral blood and bone marrow cells of animals after a flight in Cosmos-936.

Methods

Experiments were conducted on male Wistar SPF mice aboard Cosmos-936 biosatellite. Experimental conditions and designations for animal groups are described in [6]. We examined 20 animals which spent 18.5 days in weightlessness (FW group) and 10 rats submitted to artificial gravity (1 G) using an onboard centrifuge (FC group).

The program of hematological studies included tests to determine the quantity of hemoglobin, erythrocytes, hematocrit, eosinophils and reticulocytes by the conventional methods in laboratory practice; the leukocyte formula was determined (on R+0, R+3 and R+24) and myelograms taken of sternal punctates (on R+0 and 24th postflight day). Hemoglobin content was determined in each separate erythrocyte by the interferometric method [7]. Peripheral blood erythrocyte resistance was assessed in vitro according to curves of osmotic hemolysis in solutions of sodium chloride of descending concentrations, from 0.60 to 0.48%.

Using a scanning attachment to the EM-100C electron microscope, a quantitative and qualitative assay was made of different forms of erythrocytes [8] on the 24th day of the recovery period.

We followed an analogous system in the ground-based synchronous experiment (SC group).

Results and Discussion

Examination of animals in experimental FC and FW groups in the first postflight hours enabled us to demonstrate a reliable increase in hemoglobin and erythrocyte content, as compared to control levels (Figure 1). Table 1 lists data on changes in peripheral blood leukocytes. We were impressed by the development of leukopenia, eosinopenia, lymphopenia and neutrophilia in peripheral blood of FW group rats.

Table 1. Changes in rat peripheral blood leukocytes at different postflight times

GROUP	LEUKOCYTES, THOUS/MM^3			SEGMENTED NEUTROPHILS, %			LYMPHOCYTES, %			EOSINOPHILS, PER MM^3		
	POSTFLIGHT DAYS											
	0	3	25	0	3	25	0	3	25	0	3	25
FW	5,90** ±0,91	9,80* ±0,84	8,70 ±0,37	45,00** ±7,68	22,00 ±2,76	10,60 ±1,72	50,00** ±7,30	70,00 ±2,0	80,60 ±1,93	16,00** ±3,74	62,00 ±7,50	114 ±13,45
FC	8,10 ±0,47	9,80* ±0,63	9,10 ±0,61	22,00* ±1,92	22,00 ±3,09	10,40 ±1,63	73,00 ±1,82	73,00 ±3,24	83,60 ±1,16	24,00* ±3,78	62,00 7,60	113,00 20,35
SC	6,90* ±0,31	7,80 ±0,93	9,50 ±0,73	20,00 ±0,95	16,60 ±4,42	12,80 ±2,70	78,00 ±0,58	78,60 ±4,54	81,00 ±2,81	24,00* ±3,38	37,00* ±5,20	103,00 ±9,92
VC	8,10 ±0,43	6,60 ±0,08	8,20 ±0,70	16,0 ±1,67	—	10,00 ±1,03	79,00 ±1,93	—	83,60 ±0,97	52,00 ±9,64	72,00 ±12,74	106,00 ±12,21

*Here and in Table 2, differences are significant (P<0.05) in relation to VC [vivarium control] group.

**Significant (P<0.05) differences from FC group.

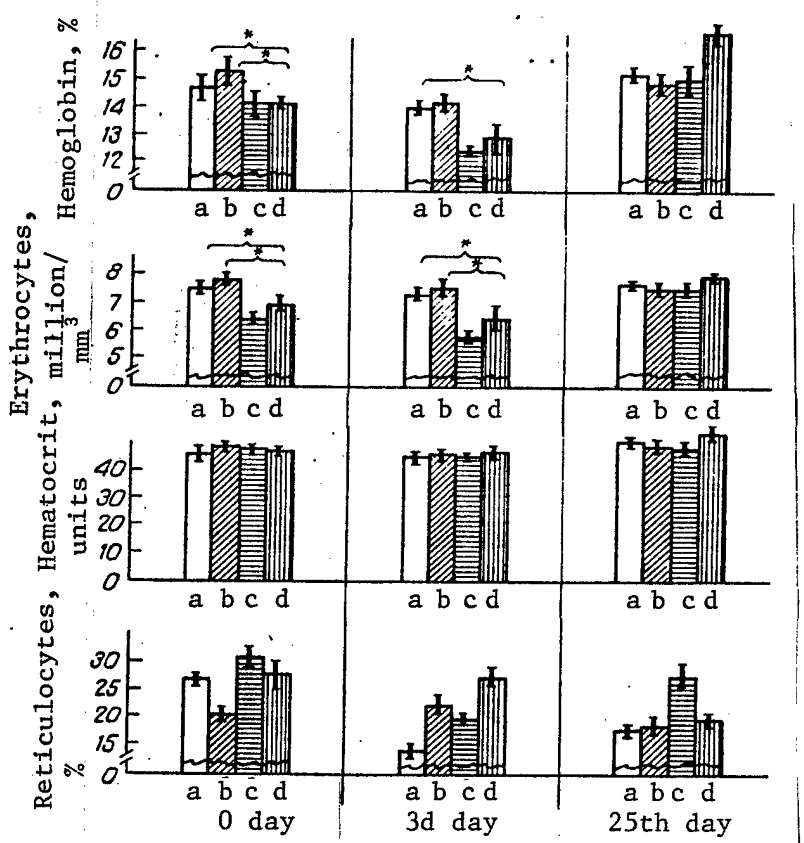

Figure 1. Changes in rat peripheral blood parameters at different times after flight in Cosmos-936

a, b, c, d) FC, FW, SW [synchronous experiment, weightlessness] and VC.

The braces show statistically significant differences in mean values.

These signs were less marked in the FC group of animals.

Neutrophil and lymphocyte content in SW group animals did not differ from the vivarium control (VC) throughout the recovery period.

Examination of animals on the 3d postflight day revealed a tendency toward normalization of morphological composition of blood, and on subsequent days these parameters remained within the range inherent in this animal species under normal conditions.

At these times we failed to demonstrate appreciable differences in hematocrit parameters between different groups of animals. On 0 day, there was some decrease in reticulocytes in the blood of FW group rats, as compared to the FC and VC groups (see Figure 1).

Table 2. Osmotic resistance of erythrocytes from rats flown in Cosmos-936

RECOVERY PERIOD, DAY	RAT GROUP	ERYTHROCYTE RESISTANCE, % WHOLE ERYTHROCYTES IN SOLUTIONS WITH CONCENTRATIONS OF 0,48	0,50	0,52	0,54	0,60
3	FW	5,6±0,5 $P<0{,}02$*	13,5±0,9	19,4±1,8	23,8±1,0 $P<0{,}01$*	65,1±5,3
	FC	8,8±1,6	15,4±1,7	22,3±3,1	27,5±3,2	67,1±4,1
	VC	8,5±0,7	14,3±0,9	24,2±3,0	35,3±3,1	62±4,9
6	FW	7,2±1,1	13,9±1,2	25,1±2,8	25,2±2,5	65,9±4,9
	FC	11,8±1,5 $0{,}15<P<0{,}05$*	18,0±2,5	25,1±2,8	39,1±4,7 $0{,}1<P<0{,}05$*	75,3±6,9
	VC	8,1±1,0	14,6±1,8	19,3±2,0	27,2±1,9	69,1±4,9
24	FW	8,1±1,0	16,2±1,9	25,3±1,8	41,1±1,1	77,6±4,3
	FC	9,0±2,1	16,6±2,4	25,5±3,4	34,0±3,9	76,9±2,7
	VC	9,9±0,9	15,6±1,0	24,4±1,4	38,8±2,9	78,4±3,7

On the 3d day, the FW group of animals presented a decrease in osmotic resistance of erythrocytes, as compared to the VC group (Table 2). This decline was brief; already on the 6th postflight day the difference between these groups of animals disappeared.

The findings were different in the FC group of rats: on the 3d postflight day they showed no decrease in osmotic resistance of erythrocytes such as found in the FW group.

On the 24th postflight day, no differences were demonstrable between FW and VC groups of animals with regard to parameters characterizing osmotic resistance of erythrocytes.

There was no change in erythrocyte resistance in the SW group of animals.

Interference microscopy was used to determine the amount of solid substances in peripheral blood erythrocytes.

In healthy control animals, average solid matter content was 19.9±0.3 pg. The percentage of erythrocytes with dry mass of 10-20 g and 20-30 pg is typical of the physiological scatter in amount of solid erythrocyte substance in the VC group of rats.

After returning to earth, we failed to demonstrate any appreciable differences in amount of solid matter in the bulk of erythrocytes in rats referable to FW and FC groups, nor between these groups of rats and the control. The observed changes could be attributed to individual physiological fluctuations.

On R+24, we examined peripheral blood erythrocytes under a scanning electron microscope in order to detect changes in shape of erythrocytes. We found that, in all instances, there was prevalence of erythrocytes in the form of a biconcave disk with smooth surface (discocytes).

In blood samples from FC group animals, 93% of the erythrocytes had a discoid shape and 7% were in the form of discocytes with one process or crest; in the FW

group, 90% were discocytes, 8.5% were discocytes with processes and 1.5% had an altered shape in the form of a deflated ball.

In VC animals, there were 89% discocytes, 9.5% discocytes with a process and 1.5% of the erythrocytes had the shape of a deflated ball. Neither the shape nor architectonics of erythrocytes of experimental groups of animals showed differences from the findings in control rats.

The bone marrow taken from the sternum of animals in the FW and VC groups on 0 day of the recovery period was characterized by some decrease in elements of erythroid hemopoiesis and the lymphocyte class (the difference was statistically unreliable). The percentage of proliferative cells and granulocytes was elevated in the FW group of animals at the expense of eosinophil and neutrophil myelocytes, as compared to figures for VC rats ($P<0.01$; Figure 2).

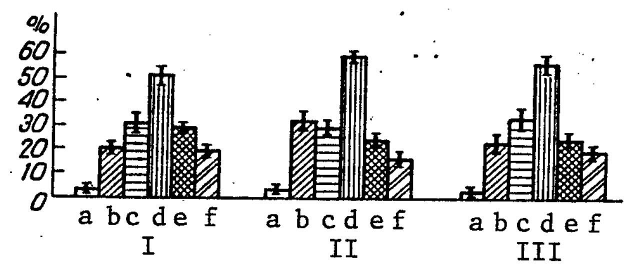

Figure 2. Morphological composition of rat bone marrow on 0 day.

Y-axis, percentage of cells

I-III) VC, FC and FW groups, respectively

a) reticular cells
b) proliferative cells in granulocyte class
c) differentiated cells in granulocyte class
d) granulocyte class cells
e) erythroid class cells
f) lymphoid cells

However, the increase in proliferative granulocyte type cells was more marked in the FW group of rats.

Toward the end of the readaptation period there was restoration of proportions between bone marrow cells in all groups of animals.

Analysis of experimental data enables us to note that the FC group of animals endured weightlessness better. They did not present a severe stress reaction, their hematological parameters reverted rapidly to normal. Since the extreme factors related to biosatellite launching and landing were the same for animals in the FW and FC groups, while decreased erythrocyte resistance was demonstrated only in the FW group, it can be considered that this decline was caused by weightlessness and, perhaps, the change from weightlessness to earth's gravity.

Our findings are consistent with the results reported in [5], where a study was made under identical conditions of spontaneous hemolysis in vivo and a significant increase was demonstrated.

Evidently, weightlessness does not diminish saturation of erythrocytes with hemoglobin. We failed to demonstrate reliable intergroup differences in interferometry of their dry mass.

The increase in percentage of young granulocyte series cells, which was noted in FW group animals, was not found in the FC group.

A comparison of the results of the experiments aboard Cosmos-605 and Cosmos-782 to the results of our studies leads us to conclude that the stress reaction present on R+1 was more marked in the FW group of animals than in FC rats. The relatively rapid recovery of hematological parameters to normal levels is indicative of absence of functional changes in blood cells of experimental animals.

The parameters characterizing erythrocyte hemolysis are consistent with the data obtained in the Cosmos-782 experiment, where a tendency toward decline of osmotic resistance and increase in spontaneous hemolysis was demonstrated.

In conclusion, it should be noted that spaceflight conditions lead to development of a marked stress reaction and decrease in erythrocyte resistance. There was no appreciable change in levels of erythrocytes, hemoglobin, reticulocytes and hematocrit.

The findings are indicative of the preventive effect of artificial gravity: less marked development of stress reaction and it prevents decrease in osmotic resistance of erythrocytes.

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ACTIVITY OF SOME ENZYMES IN RAT LIVER SUBCELLULAR FRACTIONS AFTER FLIGHT ABOARD COSMOS-1129 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 22 Mar 82) pp 65-67

[Article by R. A. Tigranyan, Ye. G. Vetrova, S. Abraham, C. Lin, H. Klein and C. Wolkmann (USSR and United States)]

[English abstract from source] The activities of malate, isocitrate and lactate dehydrogenases were measured in the liver mitochondrial and cytoplasmatic fractions of rats flown for 18.5 days onboard Cosmos-1129. The activities of the oxidative enzymes, malate and isocitrate dehydrogenases, in the mitochondrial fraction and those of the glycolytic enzyme, lactate dehydrogenase, in the cytoplasmatic fraction were found to decrease.

[Text] Data were obtained on the effect of spaceflight factors on activity of enzymes of oxidative metabolism in blood serum, subcellular liver fractions and myocardium of rats in ground-based experiments simulating the effect of weightlessness on man and animals (hypokinesia, water immersion), as well as manned spaceflights and in the experiment aboard Cosmos-936 [1].

Our objective here was to further investigate the effect of extreme spaceflight factors on oxidative metabolism in the rat liver after a flight in Cosmos-1129 biosatellite. We assayed the activity of the main enzymes of the Krebs cycle--NAD-dependent malate dehydrogenase (MDH) and NADP-dependent isocitrate dehydrogenase (ICDH) in the mitochondrial and cytoplasmic fractions, and activity of the glycolytic enzyme, lactate dehydrogenase (LDH), in the cytoplasmic fraction of the rat liver.

Methods

Studies were pursued on rats that were divided into the following groups: F_1--animals flown in the biosatellite and decapitated 6 h after landing; their control consisted of animals in vivarium control and synchronous experiment groups (V_1 and S_1, respectively); F_2--animals decapitated 6 days after landing (control--V_2 and S_2 groups); F_3--rats that were submitted to repeated postflight immobilization stress then decapitated after 6 days (control--V_3 and S_3); F_4--animals that were decapitated 27 days after landing (control--V_4 and S_4). The mitochondrial and cytoplasmic fractions of the liver were isolated from a homogenate prepared in

0.25 M saccharose in a ratio of 1:3. The liver homogenate was centrifuged at 800 G for 10 min. The nuclei were then discarded, while the supernatant was centrifuged at 4500 G for 30 min. The formed precipitate (mitochondrial fraction) and supernatant (cytoplasmic fraction) were frozen.

For determination of specific activity of enzymes, we used the mitochondrial fraction submitted to dialysis against 0.01 M tris-HCl, pH 7.6., for 1.5 h and cytoplasmic fraction. MDH activity was determined by enzymospectrophotometry [2], ICDH by spectrophotometry [3] and LDH according to Wroblewsky et al. [4]. The protein concentration was assayed by the method of Lowry et al. [5].

Results and Discussion

Immediately after the flight, there was a decline in MDH and ICDH activity in the mitochondrial liver fraction, by 25 and 47%, respectively, as compared to parameters for rats in the vivarium control and flight group on the 6th postflight day (Table 1). In the mitochondrial fraction of the liver of rats used in the synchronous experiment, 18 and 47% decline was demonstrated immediately after its termination in activity of MDH and ICDH. These changes were reliable only for ICDH in relation to parameters of rats in the vivarium control and synchronous experiment 6 days after its termination (see Table 1). On the 6th postflight day, there was normalization of MDH and ICDH activity in mitochondrial fraction of the liver in rats flown in the biosatellite and those used in the synchronous experiment, and they reached the values for activity of these enzymes in the vivarium control group of animals. By the 27th postflight day, no changes were demonstrable in activity of the tested enzymes of oxidative metabolism (see Table 1).

Table 1.
MDH and ICDH activity in mitochondrial fraction of rat liver (M±m)

ANIMAL GROUP	MDH, NADH/MG PROTEIN/MIN	ICDH, NADP/MG PROTEIN/MIN
V_1	3,89±0,31	0,22±0,04
F_1	2,94±0,23	0,12±0,01
S_1	3,21±0,27	0,12±0,01
V_2	4,04±0,10	0,22±0,05
F_2	3,84±0,27	0,27±0,04
S_2	3,95±0,65	0,28±0,05
V_3	3,84±0,13	0,20±0,04
F_3	3,40±0,38	0,28±0,04
S_3	3,23±0,51	0,26±0,07
V_4	4,38±0,41	0,21±0,05
F_4	3,79±0,34	0,25±0,08
S_4	3,06±0,31	0,27±0,07
	$F_1 : V_1 < 0{,}05$ $F_1 : F_2 < 0{,}05$	$F_1 : V_1 < 0{,}05$ $F_1 : F_2 < 0{,}05$ $S_1 : V_1 < 0{,}05$ $S_1 : S_2 < 0{,}05$

We failed to demonstrate changes in MDH and ICDH activity in the cytoplasmic liver fraction of rats flown in space and used in the synchronous experiment, as compared to vivarium control animals and those tested 6 days after the flight (Table 2). In the cytoplasmic liver fraction of rats in the synchronous experiment, there was reliable decrease in LDH activity, as compared to animals in the vivarium control, and this decline was demonstrated at all stages of the experiment. Immediately after landing, we failed to demonstrate a decrease in LDH activity in the cytoplasmic liver fraction of rats in the flight group; by the 6th postflight day, this parameter was reliably lower than in animals of the analogous vivarium control group (see Table 2).

Extreme factors, in the form of repeated 2.5-h immobilization stress for 6 postexperiment days, did not

Table 2.
MDH, LDH, ICDH activity in rat liver cytoplasmic fraction (M±m)

ANIMAL GROUP	MDH, NADH/ MG PROTEIN/ MIN	ICDH, NADP/ MG PROTEIN/ MIN	LDH, NADH/ MG PROTEIN/ MIN
V_1	3,74±0,21	0,31±0,02	13,6±0,4
F_1	3,64±0,15	0,35±0,03	13,4±0,8
S_1	3,55±0,44	0,30±0,03	10,8±0,6
V_2	3,69±0,25	0,29±0,04	13,8±0,3
F_2	3,30±0,21	0,33±0,01	11,9±0,6
S_2	3,73±0,40	0,31±0,02	10,7±0,6
V_3	3,73±0,27	0,31±0,01	13,4±0,2
F_3	3,44±0,17	0,33±0,01	11,1±0,3
S_3	3,12±0,24	0,30±0,02	10,7±0,4
V_4	3,83±0,28	0,30±0,03	13,7±0,2
F_4	3,84±0,58	0,44±0,10	13,9±2,2
S_4	3,71±0,52	0,32±0,03	10,1±0,7

$S_1 : V_1 < 0{,}01$
$S_2 : V_2 < 0{,}001$
$S_3 : V_3 < 0{,}001$
$S_4 : V_4 < 0{,}001$
$F_2 : V_2 < 0{,}05$
$F_3 : V_3 < 0{,}001$

have an appreciable effect on activity of the tested enzymes in either the vivarium control or flight group, or in the synchronous experiments (see Tables 1 and 2).

It is apparent from the submitted data that the main changes were referable to oxidative enzymes, MDH and ICDH, in the mitochondrial fraction and the glycolytic enzyme, LDH, in the cytoplasmic fraction of the liver. Studies pursued aboard Cosmos-936 demonstrated a decrease in MDH and ICDH in the cytoplasmic fraction of flight group animals, both in weightlessness and with creation of artificial gravity aboard the biosatellite, with unchanged activity of these enzymes in the mitochondrial fraction. Evidently, this change in activity of oxidative enzymes was due to the specific spaceflight factors, since no changes in activity of these enzymes were demonstrable in animals used in the synchronous ground-based experiment.

The data we have submitted here differ from findings obtained in studies referable to the preceding biosatellite. Since there was demonstration of similar dynamics of changes in activity of MDH, ICDH and LDH in the flight and synchronous experiments, it can be assumed that they were not attributable to the specific effect of flight, but to factors associated with the flight, such as, for example, change in gas environment in the spacecraft cabin, in particular, the elevation of CO concentration in the biosatellite's atmosphere, which elicited relative tissue hypoxia in the animals.

As shown by data published previously [6], in the presence of hypoxic hypoxia one observes a drastic drop of liver MDH level, mainly referable to the cytoplasmic fraction of this enzyme. In our experiment, the specific form of hypoxia that appeared under the effect of CO led to decrease in overall MDH activity at the expense of the mitochondrial form of the enzyme, with retention of the level of this enzyme in cytoplasm, which could lead to depression of redox processes in the Krebs cycle in liver cells. Some discrepancy in the obtained results is apparently due to the specific effect of hypoxia on hepatic tissue.

The decline in LDH activity in the cytoplasmic fraction of liver cells causes a decrease in glycolytic processes. According to the data of L. Ye. Panin [7], under stress there is intensification in the liver of processes of de novo glucose synthesis from proteins and (in part) fats, i.e., from an organ that utilizes glucose, the liver changes into an organ that synthesizes it. Inhibition of the process of glycolysis and intensification of processes of

gluconeogenesis in the liver are instrumental in increasing delivery to the brain of carbohydrate substrates. Glycerin, amino acids and lactate are the main precursors of glucose synthesis in the liver [8]. The decrease we demonstrated in LDH activity of the cell cytoplasm reduces the change of lactate into pyruvate and, consequently, is instrumental in accumulation of lactate, i.e., it creates conditions for intensification of gluconeogenesis.

Thus, the results obtained from the experiment in Cosmos-1129 indicate, on the one hand, that there is depression of processes of substrate oxidation in the Krebs cycle by liver cell mitochondria and, on the other hand, depression of glycolytic processes in the cytoplasm and, perhaps, intensification of gluconeogenesis.

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EFFECT OF HYPOKINESIA ON VITAMIN D METABOLISM IN RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 14 May 82) pp 68-73

[Article by I. N. Sergeyev, Yu. P. Arkhapchev, V. B. Spirichev, A. S. Ushakov, M. S. Belakovskiy, L. F. Linberg, N. V. Blazheyevich, S. V. Sokolova and V. A. Yurkiv]

[English abstract from source] The effect of short- (7 days) and long-term (28 days) hypokinesia on 25-oxycholecalciferol metabolism was investigated in rats that were fed diets containing adequate amounts of vitamin D, calcium and phosphorus. Eighteen hours before sacrifice the animals were injected ^{3}H-25(OH)D_3. ^{3}H-metabolites of D_3 formed in vivo were separated by high-performance liquid chromatography, and their concentrations in the serum, kidneys, intestinal mucosa and bones were measured. Long-term hypokinesia decreased the content of ^{3}H-1,25(OH)$_2D_3$ and increased that of ^{3}H-24,25(OH)$_2D_3$ in the serum and kidneys. The exposure diminished the content of both ^{3}H-1,25(OH)$_2D_3$ and ^{3}H-24,25(OH)$_2D_3$ in the intestinal mucosa and bones and increased that of nonmetabolized ^{3}H-25(OH)D_3. The data obtained are indicative of a lower synthesis of 1,25(OH)$_2D_3$ and a higher synthesis of 24,25(OH)$_2D_3$ in the kidneys, as well as of a reduced binding of 24,25(OH)$_2D_3$ in the intestinal mucosa and bones in hypokinetic rats. Possible causes of variations in the biosynthesis of vitamin D active metabolites and their contribution to the disorders of calcium metabolism and bone density during hypokinesia are discussed.

[Text] The hormonal system, which includes parathyroid hormone, vitamin D and calcitonin, maintains homeostasis of calcium and structural integrity of bone [1]. The original vitamin D has no appreciable biological activity per os, but functions only after conversion into active metabolites. In the liver, vitamin D_3 is hydroxylated to 25(OH)D_3, which is the transport form of this vitamin. Then 25(OH)D_3 is metabolized to dihydroxy derivatives of D_3: 1,25(OH)$_2D_3$ and 24,25(OH)$_2D_3$.* These metabolites are synthesized in the

*Abbreviations used: D_3--vitamin D_3, cholecalciferol; 25(OH)D_3--25-hydroxycholecalciferol; 1,25(OH)$_2D_3$--1,25-dihydroxycholecalciferol; 24,25(OH)$_2D_3$--24,25-dihydroxycholecalciferol.

kidneys. The mucosa of the small intestine, cartilage and bone are capable of producing $24,25(OH)_2D_3$, whereas synthesis of $1,25(OH)_2D_3$ occurs only in the kidneys [3]. As it is now believed, $1,25(OH)_2D_3$ is a hormonal form of vitamin D_3. The main function of $1,25(OH)_2D_3$ is to raise the calcium and phosphate levels in blood and extracellular fluid to physiological supersaturated concentrations, which are necessary, in particular, for normal mineralization of de novo formed bone. Here, $1,25(OH)_2D_3$ increases the concentrations of calcium and phosphate in blood, stimulating active transport of these ions into the small intestine, their resorption in the kidneys and mobilization from preformed bone tissue [4].

Unlike $1,25(OH)_2D_3$, the functions of $24,25(OH)_2D_3$ are less apparent. In the above-mentioned processes, $24,25(OH)_2D_3$ activity is lower than that of $1,25(OH)_2D_3$ (with administration of equimolar doses of these metabolites to nephrectomized vitamin D deficient animals). However, there is rigid regulation of $24,25(OH)_2D_3$ synthesis in the body within the range of circulating concentrations that exceed by 50-100 times the $1,25(OH)_2D_3$ level. It was demonstrated in several studies of recent years that $24,25(OH)_2D_3$ has more biological activity than has been formally assessed, and it is probably a functionally active form of vitamin D_3 that regulates ossification [6-11].

Circulating concentrations of parathyroid hormone, calcium, phosphorus, as well as $1,25(OH)_2D_3$ itself, are the chief factors that regulate vitamin D metabolism in the body [12].

Prolonged restriction of movement leads to impairment of calcium metabolism and condition of bone tissue [13]. The role of vitamin D in development of these changes has not been investigated. For this reason, our objective here was to study formation of $1,25(OH)_2D_3$ and $24,25(OH)_2D_3$ from their precursor, $25(OH)D_3$, in hypokinetic rats.

Methods

In our experiment we used male Wistar rats weighing 215 ± 2.4 g. The animals were given a semisynthetic diet with 0.6% calcium, 0.6% phosphorus [14] and water ad libitum. To create hypokinesia, the animals were kept in adjustable ["compressible"] cages. Metabolism of $25(OH)D_3$ was examined after 7 and 28 days of hypokinesia. The animals were given intraperitoneal injections of 25-hydroxy [26(27)-methyl-^{3}H] cholecalciferol (^3H-$25(OH)D_3$, with specific activity of 7.7 Ci/mmol; Radiochemical Center, Amersham, England) in 0.1 mℓ of a mixture of ethanol and propylene glycol (1:4) in a dosage of 1.0 or 1.5 μCi/animal (on day 7 or 28, respectively). The animals were decapitated after 18 h, the superior segment of the intestine, 30 cm in length, was isolated, as well as both kidneys and femurs. The segments of intestine and kidneys, after removal of capsule, were washed in cold saline. The mucosa was scraped off with a slide. The mucous membrane of the kidneys and femurs, from which muscles and bone marrow were removed, were weighed, then the mucosa and each kidney were homogenized for 1.5 and 2 min with a glass pestle in 3 mℓ methanol. The femurs were ground in a mortar, frozen in liquid nitrogen and washed off in 3 mℓ methanol. Blood was centrifuged after 2-3 h. We added 3 mℓ methanol to 1 mℓ serum. To methanol extracts, we added authentic nonradioactive $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$ (100, 125 and 150 ng, respectively; Hoffman-LaRoche, Switzerland, United States).

We extracted from serum, kidneys, mucosa and bones the ^{3}H-metabolites of D_3 with a mixture of chloroform and methanol by the method of Bligh and Dyer [15]. All of the organic solvents used in the experiment were purified by double distillation, while hexane to be used for high-performance liquid chromatography was additionally treated on silicagel L 40/100 (CSSR). We added to methanol extracts 3 mℓ chloroform and, having thus obtained a single-phase system, allowed it to stand overnight at room temperature. We then added 3 mℓ chloroform and 1.5 mℓ 2% Na_2CO_3 solution to produce a two-phase system, mixed it in a Vortex-Mix mixer for 15 min and centrifuged it for 15 min at 3000 G. The organic phase was removed, and the aqueous phase was extracted again with 5 mℓ chloroform. The combined organic extracts were evaporated under vacuum at a temperature not exceeding 40°C. In order to assay overall radioactivity, we took samples of 150 μℓ from the combined organic extract and aqueous phase after re-extraction. Radioactivity of aliquots of aqueous phase was measured with a Bray scintillation counter. The degree of extraction of ^{3}H-metabolites of D_3 from serum, kidneys, mucosa and bones constituted 97.2±1.1, 88.7±2.7, 89.2±4.4 and 81.8±4.0%, respectively. There were no differences in degree of extraction between groups.

Preliminary chromatographic purification was performed on a Prep-I (DuPont, United States) sample processor with 12-column rotor. The chromatography columns were filled with silica gel L 40/100 and L 5/40 (5:1), washed with 2 mℓ of a mixture of hexane, methanol and chloroform (9:1.4:1 by volume) and 5 mℓ hexane. After evaporation the dry residue was washed off twice on a column of 2 mℓ hexane and eluated in 1 mℓ mixture of hexane, methanol and chloroform (9:1.4:1). The fractions were discarded. Then 10 mℓ of this mixture was used to flush out the fraction containing $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$, which was evaporated to a volume of 0.5 mℓ, transferred into tapered 0.65-mℓ vials (Reacti Vials), evaporated until dry, dissolved in 50 μℓ of a mixture of hexane and isopropanol (88:12 by volume) and put entirely into the chromatograph. Some of the samples were dissolved in 60 μℓ of this mixture, and 10 μℓ was taken to count overall radioactivity. The total yield of ^{3}H-metabolites of D_3 (extraction, preliminary chromatographic treatment, transfer to Reacti vials) constituted 75.5±1.7, 66.4±2.2, 71.9±5.0 and 62.1±5.9% for serum, kidneys, mucosa and bones, respectively.

We preparatively isolated ^{3}H-metabolites of D_3 by high-performance liquid chromatography (HLC), for which purpose we used the system for HLC of the Altex Co. (United States): liquid chromatograph with loop 50 μℓ in volume, high-performance Ultrasphere Si column, 5 μm, 4.6×250 mm, ultraviolet Hitachi 100-40 detector with Altex 155-00 grid and a Linear recorder. The eluation system consisted of hexane and isopropanol (88:12 by volume), flow rate was 1 mℓ/min and pressure was 40 atm. The peaks of authentic nonradioactive metabolites used to identify each radioactive peak were recorded using a UV [ultraviolet] detector (λ = 265 nm, sensitivity 0.04 A on the complete scale, tape feeding rate 0.5 cm/min). The retention time was 5, 7 and 15 min for $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$, respectively (Figure 1). The described chromatographic pretreatment and HLC methods were developed with use of the data of Gilbertson and Stryd [16], Jones and DeLuca [17].

We took 8 fractions for analysis of each sample; peaks corresponding to $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$ were collected entirely in separate vials. The solvent of each fraction was evaporated and we added 5 mℓ scintillator (2 g PPO and 100 mg POPOP/ℓ toluene) to the dry residue. Radioactivity was measured

with a Mark-III (model 6880, Searle-Analytic, FRG) liquid scintillation counter in the ^3H channel. Quality of counting constituted 55%. In each sample, we found 3 radioactive peaks corresponding to authentic nonradioactive $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$ (see Figure 1). Radioactivity of fractions that did not contain ^3H-$25(OH)D_3$ and ^3H-$24,25(OH)_2D_3$ and ^3H-$1,25(OH)_2D_3$ constituted 7.24±0.44, 15.31±0.82, 23.17±1.05 and 20.51±1.78% of total radioactivity for serum, kidneys, mucosa and bones, respectively. There were no differences between groups in amount of radioactivity in these fractions.

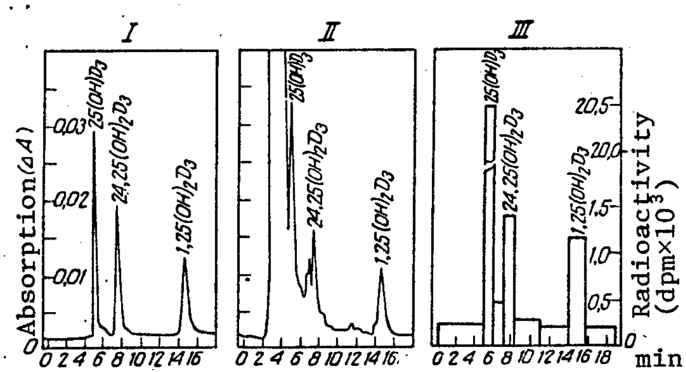

Figure 1. High-performance liquid chromatography of $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$

Chromatography conditions: high-performance Ultrasphere Si column, 5 μm, 4.6×250 mm; hexane-isopropanol (88:12 by volume); flow rate 1 mℓ/min; pressure 40 atm; sensitivity 0.04 A on complete scale; tape feeding rate 0.5 cm/min

I) chromatogram of mixture containing 100 ng $25(OH)D_3$, 125 ng $24,25(OH)_2D_3$ and 150 ng $1,25(OH)_2D_3$

II) chromatogram of purified blood serum extract containing ^3H-metabolites of D_3 and authentic nonradioactive metabolites

III) radioactivity of fractions of blood serum extract containing ^3H-metabolites of D_3

We assayed each metabolite of vitamin D_3 in decays/min/mℓ serum or g tissue (in the tables, these are expressed as percentages of their sum). We obtained analogous results when we calculated the levels of ^3H-metabolites of D_3 as percentage of overall radioactivity passed through the high-performance column.

Previously described techniques [14] were used to assay calcium, inorganic phosphorus in blood serum and changes in osseous tissue (femur).

Results and Discussion

Keeping rats in hypokinetic cages for 7 days did not elicit changes in concentration of calcium and inorganic phosphorus in blood serum (9.7±0.2 and 8.9±0.5 mg/100 mℓ, respectively versus 9.9±0.2 and 8.3±0.2 mg/100 mℓ in the control) or in bone, with the exception of a 6.2% decrease in calcium content of the femoral epiphysis ($0.05<P<0.1$).

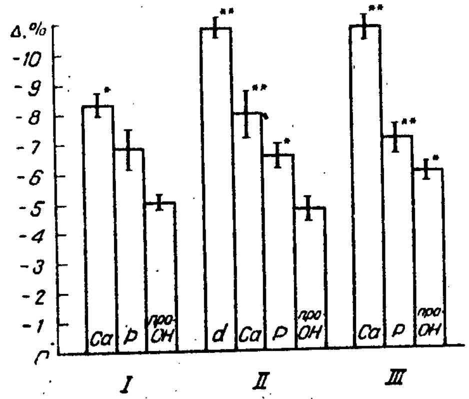

Figure 2.

Effect of 28-day hypokinesia on specific weight and chemistry of rat femur. The changes are expressed as % of control group values. Calcium, phosphorus and hydroxyproline content was assayed in mg/g dry tissue, specific weight (d) per g dry tissue/cm^3.

I) entire bone
II) diaphysis
III) epiphyses
npo OH) hydroxyproline
$*0.05<P<0.1$
$**P<0.05$

After 28 days of hypokinesia, the rats showed a decrease in serum calcium concentration (9.0±0.3 mg/100 mℓ, versus 10.1 mg/100 mℓ in the control; $P<0.01$). Blood serum phosphorus content constituted 8.7±0.4 mg/100 mℓ in hypokinetic rats and 8.2±0.2 mg/100 mℓ in control animals. Bone changes consisted of a drop in specific weight of femoral diaphyses, decrease in calcium, phosphorus and hydroxyproline content of both the whole bone and its diaphysis and epiphyses (Figure 2), which is consistent with previous findings [18]. A more marked decrease in calcium was demonstrated in the epiphyses.

We failed to demonstrate reliable changes in metabolism of ^{3}H-25(OH)D_3 in rats after 7-day hypokinesia, with the exception of some decline of ^{3}H-1,25(OH)$_2D_3$ level in the kidneys (Table 1). The approximately same percentile levels of ^{3}H-24,25(OH)$_2D_3$ and ^{3}H-1,25(OH)$_2D_3$ in the tissues examined are attributable to the similar rate of their synthesis in the kidneys [5].

Table 1. ^{3}H-metabolites of D_3 in blood serum, kidneys, mucosa of small intestine and bones of rats after 7-day hypokinesia

MATERIAL EXAMINED	ANIMAL GROUP	^{3}H-25 (OH) D_3	^{3}H-24,25(OH)D_3	^{3}H-1,25(OH)$_2D_3$	TISSUE MASS, MG
SERUM	CONTROL (5)	91,02±0,36	4,24±0,45	4,73±0,41	232±10*
	HYPOKINESIA (5)	91,26±0,62	5,20±0,75	3,53±0,70	207±24*
KIDNEYS	CONTROL (6)	82,03±0,84	7,25±0,92	10,72±0,37	746±12
	HYPOKINESIA (6)	81,96±0,95	9,60±0,96	8,44±0,79 $P<0,05$	658±11 $P<0,01$
MUCOSA	CONTROL (3)	63,63±2,72	9,46±3,13	26,91±2,74	868±118
	HYPOKINESIA (3)	67,67±2,50	9,42±1,08	22,92±2,68	773±108
BONES	CONTROL (3)	73,36±2,40	15,56±2,84	11,08±0,65	334±14
	HYPOKINESIA (3)	76,66±2,71	12,05±2,08	11,28±0,94	319±23

Note: Here and in Table 2, the amount of ^{3}H-metabolites of D_3 is expressed as % of overall radioactivity of fractions containing ^{3}H-25(OH)D_3, ^{3}H-24,25(OH)$_2D_3$ and ^{3}H-1,25(OH)$_2D_3$. The number of readings is given in parentheses. The asterisk indicates the animals' weight (g).

Prolonged hypokinesia (for 28 days) led to a drop of ^{3}H-1,25(OH)$_2D_3$ level and rise of ^{3}H-24,25(OH)$_2D_3$ level in serum and kidneys (Table 2). There was a marked negative correlation ($r = -0.62$, $n = 20$; $P<0.01$) between levels of ^{3}H-1,25(OH)$_2D_3$ and ^{3}H-24,25(OH)$_2D_3$ in the kidneys. In the small intestinal

mucosa and femurs, there was a drop in both ^3H-1,25$(OH)_2D_3$ and ^3H-24,25$(OH)_2D_3$ with increase in concentration of ^3H-25$(OH)D_3$.

Table 2. ^3H-metabolites of D_3 in blood serum kidneys, mucosa of small intestine and bones of rats after 28-day hypokinesia

MATERIAL EXAMINED	ANIMAL GROUP	^3H-25(OH)D_3	^3H-24,25$(OH)_2D_3$	^3H-1,25$(OH)_2D_3$	TISSUE MASS, MG
SERUM	CONTROL (9)	91,97±0,61	3,76±0,29	4,33±0,41	305±13
	HYPOKINESIA (7)	91,66±1,19	5,34±0,69	3,15±0,62	237±5
			$P<0,05$		$P<0,02$
KIDNEYS	CONTROL (10)	82,69±0,83	5,94±0,24	11,62±0,79	921±39
	HYPOKINESIA (10)	83,20±0,91	9,33±0,55	7,52±0,69	730±18
			$P<0,001$	$P<0,002$	$P<0,01$
MUCOSA	CONTROL (5)	61,10±3,81	9,18±0,78	30,06±3,04	909±24
	HYPOKINESIA (5)	71,17±1,67	7,30±0,58	21,52±1,46	822±56
		$P<0,05$	$0,05<P<0,1$	$P<0,05$	
BONES	CONTROL (5)	73,97±2,37	13,86±1,28	11,48±1,64	494±7
	HYPOKINESIA (5)	85,83±1,36	7,78±0,71	6,39±0,65	387±8
		$P<0,01$	$P<0,01$	$P<0,05$	$P<0,001$

In control animals, highest ^3H-1,25$(OH)_2D_3$/^3H-24,25$(OH)_2D_3$ ratio (2.84-3.27) was found in the mucous membrane and lowest in bones (0.71-0.83). Under hypokinetic conditions, this ratio dropped in serum, kidneys, mucosa and rose insignificantly in bones.

Our findings are indicative of an appreciable change in calcium metabolism and condition of bone tissue with prolonged hypokinesia. According to our preliminary data, active transport of calcium in the small intestine of hypokinetic rats was 30-40% diminished, and this preceded development of hypocalcemia. The observed changes in chemistry and specific weight of bone could be related to some increase in resorption and development of osteoporosis-type changes. Perhaps, these disturbances are also due to depression of osteogenesis. Calcium, phosphorus, hydroxyproline content and specific weight of bone increase constantly when rats grow normally. Under hypokinetic conditions, the weight of the animals and femurs increased insignificantly, and for this reason the parameters of osseous tissue determined in this experiment characterize the rat femur in the case of prolonged hypokinesia as being "younger," i.e., (in this instance) as a bone with retarded growth.

The data we obtained indicate that metabolism of 25$(OH)D_3$ changes in hypokinetic rats, which are on a diet that provides vitamin D with optimum calcium and phosphorus content. Prolonged hypokinesia led to decline of ^3H-1,25$(OH)_2D_3$ level in serum, kidneys, mucosa of the small intestine and bones. The usual reciprocal relations between 1,25$(OH)_2D_3$and 24,25$(OH)_2D_3$were observed in serum and kidneys, whereas in the mucosa and bones the level of ^3H-24,25$(OH)_2D_3$ dropped and there was accumulation of unmetabolized ^3H-25$(OH)D_3$.

It should be stressed that the observed changes in levels of ^3H-metabolites of D_3 are apparently real changes in production of 1,25$(OH)_2D_3$ and 24,25$(OH)_2D_3$ in the body, although this statement requires strict validation. At the end of the experiment, the hypokinetic animals had a lower weight than the controls and, consequently, they could have a smaller pool of circulating 25$(OH)D_3$. This

could be associated with an increase in percentage of ^3H-1,25$(OH)_2D_3$ or ^3H-24,25$(OH)_2D_3$ and drop in level of the reciprocal metabolite (in this case, elevation of ^3H-24,25$(OH)_2D_3$ level and drop of ^3H-1,25$(OH)_2D_3$ level). However, in calculating the amounts of ^3H-metabolites of D_3 in decays/min/mℓ serum or gram kidney, mucosa and bone, we observed an increase in amounts of ^3H-25$(OH)D_3$, ^3H-24,25$(OH)_2D_3$ and ^3H-1,25$(OH)_2D_3$, which was proportionate to the reduction in animal weight (the given dosage of ^3H-25$(OH)D_3$ was the same for control animals and rats kept under hypokinetic conditions). Consequently, there was apparently no appreciable decrease in circulating pool of 25$(OH)D_3$ in hypokinetic rats.

Thus, the changes in levels of ^3H-1,25$(OH)_2D_3$ and ^3H-24,25$(OH)_2D_3$ in serum and kidneys of hypokinetic rats are indicative of diminished synthesis of 1,25$(OH)_2D_3$ (by 21.3 and 35.3% after 7 and 28 days of hypokinesia) and increased synthesis of 24,25$(OH)_2D_3$ (by 24.5 and 36.3%) in the kidneys). There was accumulation of ^3H-25$(OH)D_3$ in the mucosa and bones of hypokinetic rats, which could be indicative of inhibition of production of 24,25$(OH)_2D_3$ from 25$(OH)D_3$ in these tissues (by 20.5% in the mucosa after 28-day hypokinesia; by 22.6 and 43.9% in bones after 7- and 28-day hypokinesia), and a marked decline of ^3H-24,25$(OH)_2D_3$ level was demonstrated in bones, in spite of some increase in circulating level of this metabolite. Evidently, the decline of ^3H-24,25$(OH)_2D_3$ level in the mucosa and bones was also due in part by diminished binding by 24,25$(OH)_2D_3$ receptors in these tissues, whereas the proportionate decline of ^3H-1,25$(OH)_2D_3$ level was apparently due only to diminished production of this metabolite in the kidneys.

In this experiment, we failed to demonstrate changes in 25$(OH)D_3$ metabolism that could be related to changes in concentration of calcium and/or phosphorus in serum. The decline of blood serum calcium level in hypokinetic rats did not induce production of 1,25$(OH)_2D_3$, as was observed in rats kept on low-calcium diets, in which the elevation of 1,25$(OH)_2D_3$ level in blood followed an increase in circulating level of parathyroid hormone [3].

Apparently, the change in vitamin D metabolism under hypokinetic conditions is attributable to the effect of other factors. In particular, similar changes in metabolism of ^3H-25$(OH)D_3$ were observed in hypophysectomied rats [19-22]. Administration to such animals of growth hormone restored metabolism of ^3H-25$(OH)D_3$ almost to the normal level [21, 22]. Administration of bovine growth hormone to rats immobilized for 10 days enhanced osteogenesis in bones of the supporting skeleton; however, this effect was not manifested at later stages, apparently as a result of formation of blocking antibodies and impaired transport of this hormone [23].

It may also be that ^3H-25$(OH)D_3$ metabolism is modified to some extent by a surplus of glucocorticoids [24], which is present under immobilization stress [13]. However, works of recent years have demonstrated that vitamin D metabolism does not change in the presence of hyperadrenocorticism [25, 26]. There is an increase in release of glucocorticoids for the first 1-2 weeks of hypokinesia, and metabolism of ^3H-25$(OH)D_3$ does not change appreciably during this period.

Our findings warrant the assumption that both metabolites of 25$(OH)D_3$--1,25$(OH)_2D_3$ and 24,25$(OH)_2D_3$--are necessary for homeostasis of calcium and

regulation of state of osseous tissue in hypokinetic rats. The decline of circulating $1,25(OH)_2D_3$ level leads to decrease in calcium absorption in the small intestine and hypocalcemia, which could, in part, limit mineralization of de novo formed bone. The decline of levels of both $1,25(OH)_2D_3$ and $24,25(OH)_2D_3$ in bones is apparently indicative of drastic depression of bone formation, whereas increased resorption is less likely. Our data do not enable us to determine whether hypokinesia has a direct effect on homeostasis of calcium and vitamin D metabolism or whether the effect is mediated by changes in other metabolic processes which, in turn, modify vitamin D metabolism.

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HEMODYNAMICS OF PULMONARY CIRCULATION DURING PROLONGED HYPOKINESIA (ACCORDING TO RESULTS OF MORPHOLOGICAL INVESTIGATION)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 16 Apr 82) pp 73-76

[Article by V. I. Yakovleva]

[English abstract from source] This paper presents data on pulmonary circulation of rats during prolonged hypokinesia (30 to 165 days). It was found that the hypokinetic exposure of 30 to 60 days produced venous and, in particular, capillary plethora associated with blood redistribution and pooling in the lungs. As the exposure continued, the plethora level decreased due to the development of compensatory-adaptive reactions in the lung vessels. For instance, on hypokinetic day 90 small arteries of the muscle type developed a spasm which accelerated circulation stabilization. By hypokinetic days 120-165 pulmonary circulation returned to normal due to the further development of compensatory-adaptive mechanisms in lung vessels (tendency for hypertrophy of the media of small arteries and increase of its cross-sectional area).

[Text] The question of redistribution of blood in hypokinetic animals, with horizontal arrangement of great vessels, has still not been sufficiently explored. The opinion is held that no hemodynamic changes occur in rats, since, unlike man, they retain their natural position under hypokinetic conditions [1, 2]. Nevertheless, there is an increase in diuresis and calcium excretion under hypokinetic conditions in rats, as in man. The mechanism of this phenomenon is unclear [2]. Yet, some physiological and morphological studies have been published recently, which offer data about a change in hemodynamics as a whole [3] and, in particular, the lungs [4-6]. Thus, A. A. Karimov, who injected the vessels in the pulmonary circulation of x-ray-opaque medium and made a morphometric study of veins and capillaries (change in lumen), established that there is constriction of 3d-4th-order arteries, dilatation of veins of all calibers and increase in overall area of the capillary bed in the case of hypokinesia lasting 1 to 8 weeks. These changes progressed with increase in duration of the experiment.

We did not encounter any published studies of hemodynamics as related to longer duration of hypokinesia in the literature accessible to us. Our objective

here included histological and morphological studies of pulmonary circulation hemodynamics in the course of prolonged hypokinesia.

Methods

Experiments were conducted on male Wistar rats with initial weight of 270-300 g. Hypokinesia was produced for 30 to 165 days by means of using box-cages that restricted motor activity considerably. Control animals were kept under vivarium conditions. Ether was used to sacrifice the rats. We examined the lungs of 30 animals on the 30th, 60th, 90th, 120th and 165th days of hypokinesia (6 experimental and 6 control animals at each time). After ligating the portal region, the left lung was weighed, then both lungs were fixed in 10% neutral formalin. The material was imbedded in paraffin. Preparations were stained with hematoxylin and eosin, according to Weigert, Van Gieson, a combination of Weigert and Van Gieson stains, and we ran the Perls test for iron. We used an MOV-15 micrometer for morphometry of small arteries of the muscular type on the level of the terminal and respiratory bronchioles. Vessels of this type were measured over the entire area of total sagittal sections taken from five levels of the left lung. For arteries of the round type, we measured the diameter, lumen, thickness of muscular layer and calculated the area of the cross section of the muscular tunic. To assess the functional state of arteries we calculated the Kernogen [Kernohan?] index (ratio of thickness of media to diameter of lumen), which permits differentiation between dynamic changes in vascular tonus and structural alterations [7-9]. The data were submitted to statistical processing by the method of Student.

Results and Discussion

Postmortem examination of experimental animals failed to reveal macroscopically visible distinctions in the lungs. Pathological changes (pulmonary parasites and massive pneumonia) were demonstrated in 2 out of 30 control rats.

The results of weighing the left lung revealed that its absolute mass on the 30th and 60th day of hypokinesia did not differ from the control, although the animals' weight dropped reliably ($P<0.001$) already 30 days after the start of the experiment. At later stages, there was gradual decline in absolute mass of the lungs, and the difference between means became statistically significant ($P<0.05$ with 3 months of hypokinesia and $P<0.02$ with 5 months). During the recovery [readaptation] period, the absolute mass of the lung reached the control level only after 2 months.

The relative mass of the lung showed an increase already after 60 days of hypokinesia ($P<0.05$), and continued to grow thereafter ($P<0.02$ and $P<0.001$ after 3 and 5.5 months of hypokinesia, respectively). The increase in relative mass of the lung is attributable to the fact that the drop in body weight was considerably ahead of the reduction in lung mass.

Histological examination on the 30th-60th experimental days revealed more marked venous and capillary plethora of the lungs, as compared to the control. In half the animals in the experimental group, there was particularly marked capillary plethora; in some places the capillaries were unevenly dilated and formed "lacuna-like" reservoirs overfilled with erythrocytes. Against such a

background, edema and swelling of the walls of small arteries and veins, as well as signs of perivascular edema, were observed more often than in the control. On the 90th day of the experiment, no appreciable changes were demonstrable in filling of arteries and veins of the lungs, although some animals still presented nonuniform dilatation of the capillary lumen, which was less extensive, however, than in the lungs of rats after 30-day hypokinesia. On the basis of analysis of morphometric data (see Table), it can be concluded that there was a tendency toward spasm in the fine branches of the pulmonary artery with 3-month hypokinesia, as indicated by rise of the Kernogen index in the absence of change in area of the cross section of the muscular sheath of the vessels (see Table).

Morphological characteristics of small branches of pulmonary artery as related to duration of hypokinesia

DURATION OF HYPOKINESIA, DAYS	OUTSIDE DIAMETER, μm	DIAMETER OF LUMEN, μm	THICKNESS OF MEDIA, μm	AREA OF MEDIA, μm^2	KERNOGEN INDEX (RATIO OF MEDIA THICKNESS TO DIAMETER OF LUMEN)
30:					
CONTROL	34,2±0,68	27,9±0,68	3,16±0,08	308±16	0,113±0,005
EXPERIMENT	34,3±0,70	27,8±0,52	3,27±0,08	319±13	0,117±0,002
90:					
CONTROL	35,6±0,74	29,3±0,64	3,17±0,07	320±12	0,108±0,006
EXPERIMENT	33,0±0,66	26,0±0,63	3,29±0,08	312±11	0,127±0,005
120:					
CONTROL	34,1±0,70	27,8±0,64	3,15±0,08	306±14	0,113±0,004
EXPERIMENT	34,6±0,94	27,9±1,00	3,38±0,10	331±16	0,121±0,008
165:					
CONTROL	32,5±0,80	26,7±0,69	2,90±0,08	275±10	0,109±0,004
EXPERIMENT	32,8±0,90	26,6±0,80	3,20±0,09	298±12	0,120±0,004

After hypokinesia lasting 120-165 days, the degree of filling of not only arteries and veins, but capillaries of the lungs, did not differ from the control. Examination of small arteries of the muscular type revealed that, by the 120th day of hypokinesia, there was a tendency toward hypertrophy of the media and enlargement of its cross section. These signs became even more marked by the 165th day of the experiment (see Table).

It must be stressed that we failed to demonstrate sclerotic changes in the vascular walls and stroma of the lung, even after 5.5 months of hypokinesia, unlike the findings of other authors who found signs of sclerosis already after 60-90-day hypokinesia [5, 6].

Our data indicate that hypokinesia has an effect on hemodynamics in the pulmonary circulation. Hypokinesia lasting up to 30 days leads to development of venous and, particularly, capillary plethora. Our findings in this respect conform to the data of A. A. Kasimtsev [4]. He established, as a result of morphometric studies, that there was enlargement of diameter of capillaries and capacity of the capillary bed (by 11%) in the rat lung after 4 weeks of hypokinesia; after 8 weeks, the capacity of the capillary bed diminished, but was above normal (by 4.8%).

It can be assumed that the increased venous and, particularly, capillary plethora is related to redistribution of blood and its deposition in the lungs. Our hypothesis is confirmed by the data of O. A. Kovalev et al. [3], who established that, after 7- and 30-day hypokinesia, rats develop regional redistribution of blood in several organs and tissues; in particular, there is an increase in blood content of the lungs.

Thereafter, the degree of venous and capillary plethora diminishes because of development of compensatory and adaptive reactions in the vascular system of the lungs. Thus, on the 90th day of hypokinesia there was a spasm in small muscular arteries, as indicated by the tendency toward rise of the Kernogen index. The spasm of small arteries is instrumental in stabilization capillary circulation. As duration of hypokinesia increases (120-165 days), there is normalization of circulation in the lungs by virtue of further development of compensatory and adaptive mechanisms in the vascular system of the lungs, as indicated by the tendency toward hypertrophy of the media of small arteries and enlargement of its cross section.

Not only compensatory and adaptive reactions, which develop in the vascular system of the lung, but perhaps other mechanisms aimed at reducing the total volume of circulating blood, such as increased diuresis, depression of erythroid hemopoiesis, play a part in normalizing circulation in the lungs.

In turn, the pulmonary circulation participates, at least at the early stages, in establishing a new hemodynamic level under conditions of restricted motor activity.

The dynamics of changes in the vascular system of the lungs during prolonged hypokinesia indicate that, in rats, in spite of horizontal position of vessels, there is redistribution of blood, which is associated with deposition of blood in the pulmonary circulatory system.

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ANALYSIS OF TRACE CONTAMINANTS IN ATMOSPHERE FORMED BY HABITAT ENVIRONMENT OF THE CLOSED MAN-HIGHER PLANTS-LOWER PLANTS-MICROORGANISMS SYSTEM

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[Article by T. V. Nol'de, Yu. V. Pepelyayev, O. A. Sukhorukov and Ye. Ya. Shepelev]

[English abstract from source] Trace contaminants in the air of a biological life support system which was continuously complicated were examined. Air samples were taken by cooled traps and analyzed by gas chromatography. Changes in the air of the biological life support system as a function of its structure were compared using Hamming distance and composition similarity measures. Matrices of the measures were obtained and a graph whose structure corresponded to changes in the biological life support system was constructed. During prolonged experiments trace contaminants remained relatively stable and changed when a mineralization component was attached. It is concluded that the composition and variations in the organic components of the atmosphere can be used as an integral indicator of the function of the biological life support system as a whole.

[Text] The prospects of exploring and making economic use of space and closest celestial bodies are related to the inevitable creation of biological life-support systems (BLSS) for space crews, which are based mainly on the biological circulation of matter, by analogy to the principle of existence of earth's biosphere. One of the important and, unfortunately, least studied aspects of this problem is investigation of the composition of the gas environment formed in a BLSS (as in the biosphere) due to the combined activity of its components: man, animals, plants and microorganisms. In any artificially organized habitat, the atmosphere is one of the important ecological factors and requires expressly an ecological (combined) approach to its assessment.

It is known that vital functions of organisms are associated with discharge of many volatile products, for which reason earth's atmosphere contains hundreds of organic components, in addition to the so-called respiratory gases that have been well-studied in physiology and hygiene--oxygen and carbon dioxide. It is expressly this real, multicomponent atmosphere of earth that has been historically (through evolution) assimilated by all terrestrial organisms. The

substances that are presently called atmospheric contaminants [impurities] are, in essence, normal components in natural ecosystems and BLSS models.

With a change from an artificial gas atmosphere based on mixtures of nitrogen, oxygen and carbon dioxide to the one formed naturally (biogenically) by the BLSS investigation of its organic components in the traditional toxicological and hygienic aspect acquires not only ever increasing significance, but new methodological difficulties because of the numerous components which, even in earth's atmosphere, have still been virtually left unstudied.

But, in a BLSS, another aspect of the problem arises, that of studying the composition and dynamics of organic atmospheric constituents as an integral indicator of the state of a BLSS as a whole. Apparently, this is the first time that there is such formulation of the problem with reference to BLSS.

For this reason, we have made an attempt here to provide an integral evaluation of changes that occur in the gas phase of a BLSS as related to its functional structure, i.e., as different functional elements are added to the system in the course of an experiment, each with its own specific metabolic functions, including the capacity for output or uptake of various organic components of the atmosphere.

When there is prolonged conjugate functioning of several elements of a biological model, analysis of biogenic trace impurities acquires paramount importance, not only to man's vital functions, but for maintenance of normal living conditions for the biological elements that interact with one another through the gas phase. The active role of the gas phase in interaction between elements of a closed ecological system enable us to use it as an integral characteristic of the state of the life-support system as a whole. An attempt at such systems analysis based on the results of studying trace contaminants in the gas phase formed by a BLSS is described in this article.

Methods

In the BLSS we studied, the autotrophic element was represented for the first 28 days by higher plants, which provided for atmosphere regeneration for one person. From the 30th to 35th days, the same greenhouse and algal reactors functioned at two-thirds capacity with two participants in the study.

From the 37th to 45th days, the algal element based on chlorella operated at full power. The system itself was completely closed for gas exchange, fluid exchange [metabolism] and, in part, for food. No physicochemical methods whatsoever were used to purify the air.

The concentration method with cooled traps, which has been described previously [1], was used for analysis of trace impurities in the gas phase of such a system. Gas chromatographic separation of concentrated trace impurities was performed using the same instruments and columns, under analogous conditions [1].

Results and Discussion

The Table lists the concentrations of 26 identified constituents out of the 44 observed on different days of system operation. The first two background

samples, taken at an interval of 15 days, were collected after the plant conveyer reached a plateau. For this reason, this period can be interpreted as the self-contained function of the higher plant element. The numbers of samples 3, 4 and 5 (see Table) represent trace contaminants in the man-higher plants-microorganisms gas phase at the start, middle and end of operation of the subsystem. Sample collections 6 and 7 were made after adding another person and algal reactors, after 15 days of joint intensive operation of the entire closed BLSS.

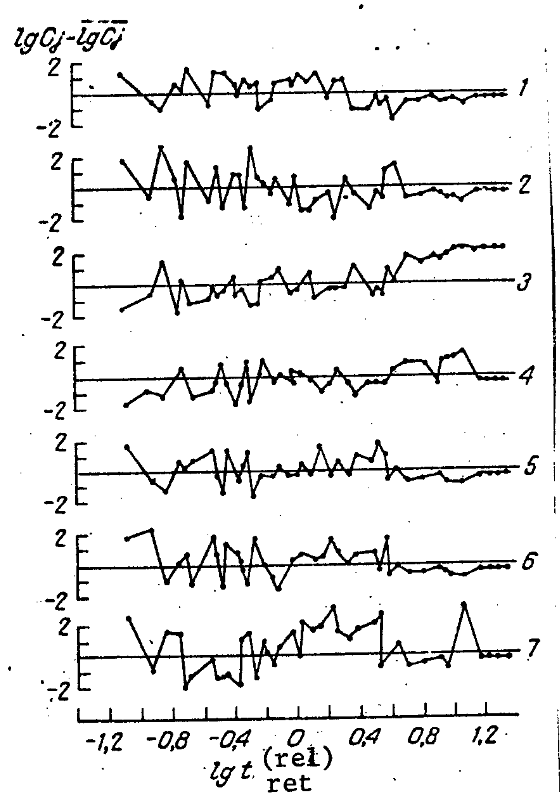
Concentration of trace contaminants (mg/m^3) in the atmosphere formed by the environment of a closed man-higher plants-lower plants-microorganisms system

No	SUBSTANCE	COMPOSITION OF SYSTEM						
		GREENHOUSE		MAN-HIGHER PLANTS-MICROORGANISMS			MAN-HIGHER PLANTS-MICROORGANISMS-ALGAL REACTORS	
		SAMPLING NUMBER						
		1	2	3	4	5	6	7
		DAY OF EXPERIMENT						
		BACK-GROUND	15	49	58	70	78	94
1	ETHANE	—	—	—	—	0,1040	0,1780	0,1960
2	PROPANE	0,0139	0,0225	0,0197	0,0099	0,4470	0,5150	0,2410
3	BUTANE	0,0369	0,1900	0,0448	0,0816	0,4850	0,7330	0,1800
4	ISOBUTANE	—	—	—	0,0700	0,0925	0,1520	0,0091
5	2,3-DIMETHYLBUTANE	0,0030	0,0536	0,0047	0,0031	0,0109	0,0066	0,0042
6	PENTANE	0,0014	0,0300	0,0281	0,0463	0,1020	0,0549	0,0350
7	ISOPENTANE	0,0084	0,0147	0,0199	0,0214	—	—	—
8	HEXANE	0,0024	0,0068	0,0090	0,0068	0,0450	0,0596	0,0871
9	HEXENE	0,0014	0,0018	0,0024	0 —	0,0044	0,0118	0,0015
10	HEPTANE	0,0027	0,0008	0,0228	0,0132	0,0171	0,0742	0,0032
11	BENZENE	0,0039	0,0080	0,0093	0,0247	0,0395	0,1110	0,0608
12	TOLUENE	0,0000	0,0960	0,0244	0,0349	0,0466	0,0813	0,0071
13	XYLENE	—	—	0,1390	0,0310	0,0110	—	—
14	OCTENE	—	—	0,0644	0,0054	—	—	0,0184
15	HEPTENE	0,0042	—	0,0047	—	—	—	—
16	METHANOL	0,0176	0,0643	0,0570	0,1690	0,1070	0,1930	0,2160
17	ETHANOL	0,0093	0,0054	0,0132	0,0214	0,3600	0,2090	0,2840
18	N-PROPANOL	0,0085	0,0092	0,0065	0,0061	0,2710	0,2750	0,0244
19	N-BUTANOL	0,0160	0,0103	0,0949	0,0189	0,1440	0,1330	0,0127
20	ISOPROPANOL	0,0406	0,2590	0,0990	0,3260	0,2530	0,6090	0,1760
21	ISOBUTANOL	0,0047	0,0079	0,0154	0,0070	0,1530	0,0000	0,0067
22	ACETONE	0,0015	0,0342	0,2880	0,0289	0,1500	0,1900	0,1170
23	ETHYLACETATE	0,0056	0,0009	0,0087	0,0069	0,0207	0,5460	0,0081
24	PROPYLACETATE	0,0103	0,0049	0,0301	0,0140	0,0987	0,1930	0,1360
25	METHYLETHYLKETONE	0 —	—	0,0031	0,0055	0,0137	0,0270	0,0074

The Table shows that, at the early stage of system operation, there is significant increase in levels of alcohols (methanol, ethanol, n-butanol, isobutanol), acetone, methylethylketone and some hydrocarbons. However, it was impossible to numerically assess from such data the changes in behavior of the system under study as it became increasingly complex.

The Figure illustrates curves of deviations from mean value of $\log C_j - \overline{\log C_j}$ as a function of $\log t_{ret}$, where C_j is the concentration of the jth component,

t_{ret} is time it is retained in relation to benzene, $\overline{\log C_j}$ is mean concentration of jth component in all 7 collections of gas phase samples.



Deviation from mean value of $\log C_j - \overline{\log C_j}$ as a function of relative time of retention $\log t_{ret}^{rel}$

1-7) numbers of collections of gas phase samples

In curve form the data are more graphic. We find that there is an increase in deviation from mean values for components with $\log t_{ret}<0$ on the last days of system operation, whereas for heavy components, with $\log t_{ret}>0.6$, maximum deviations from the mean were obtained in samplings 3 and 4. It is difficult to systematize a description of system behavior from the graphic data due to the large number of measurements (points).

For integral quantitative evaluation of the description of the BLSS, we used one of the clustering methods used for pattern recognition in the systems classification approach [2].

We consider any change in composition of the gas phase to be a vector in the tag space $\vec{X}_i\{x_{i1}\ x_{i2}\ x_{i3} \ldots x_{ij}\}$ where i = 1, 2, ... 7 is the sequential number of gas sampling, i.e., number of state of the system; the above-mentioned coordinates are components of the vector, where j is component number. The difference between two vectors X_i and X_k was determined by Hamming's distance measurement [3]:

$$D_{ik} = \sum_{j=1}^{\bar{n}} |x_{ij} - x_{kj}|.$$

According to the results of gas chromatographic analysis, obtained on a column with 15% squalane [?] on Celite 545 AW 80-100 mesh, we constructed a matrix of distances between vectors--tags of states. We took into consideration all detected components without identification. We obtained the following matrix of distances:

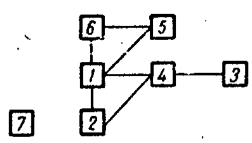
j, i =	1	2	3	4	5	6	7
1	0	0,83	1,56	0,75	0,63	0,83	1,1
2		0	1,45	1,01	1,09	1,14	1,37
3			0	0,89	1,47	1,49	1,74
4				0	0,84	1,08	1,35
5					0	0,57	1,10
6						0	0,21
7							0

In the literature, the concept is used of measure of similarity of vectors $A_{ik} = 1 - D_{ik}/D_{max}$, where D_{max} is maximum observed distance between vectors throughout the period of studying the system (in our instance, $D_{max} = 1.74$), i and k are numbers of samplings.

A magnitude of similarity that equals 1 corresponds to an identical state. The closer the resemblance is to 1, the more similar are the systems under study. Let us transform the similarity matrix in such a way that identical states would be on a diagonal and, the greater the similarity, the closer this state is to the diagonal (diagonalization of matrix). Then the matrix of similarity would have the following appearance:

$i, k =$	6	5	1	4	2	7	3
6	1	0,67	0,52	0,38	0,34	0,30	0,14
5		1	0,64	0,52	0,37	0,37	0,16
1			1	0,57	0,52	0,37	0,10
4				1	0,42	0,22	0,49
2					1	0,21	0,17
7						1	0,00
3							1

If we consider 0.4 to be the threshold of measure of similarity and consider that states for which similarity equals 0.4 are similar, we can express the relationships between states in the form of a graph, at the peaks of which are the points of samplings, while the arms link "similar" states with A>0.4:



We see that states 1, 2, 4, 5, 6 are similar to one another, states 3 and 7 are far from this group, although 3 still has a link with 4. Such a scheme graphically shows that the composition of impurities in the atmosphere, in this experiment, was stable; however, when the composition of the system was impaired there was derangement of composition of the gas phase. After discarding sampling 3 there is drastic disturbance [derangement] with rapid return to the basic state. Indeed, sampling 3 was effected after adding the mineralization element. Sampling 7 was taken on the 15th day of operation of all elements (higher plants, algal reactors and mineralization element), and it shows slow derangement of the system, which apparently was not terminated in the described experiment.

Thus, the proposed approach method, which utilizes the gas phase as an integral characteristic of the state of a complex BLSS makes it possible to numerically assess the state of the system and to track all of the cycles of its development.

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EFFECT OF PHYTONCIDES ON CEREBRAL CIRCULATION IN FLIGHT CONTROLLERS DURING PROFESSIONAL WORK

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 4 Mar 82) pp 80-83

[Article by Ya. S. Leshchinskaya, N. M. Makarchuk, A. F. Lebeda, V. V. Krivenko, A. K. Sgibnev and T. S. Bagatskaya]

[English abstract from source] In order to optimize the environment in which flight controllers normally work, volatile phytoncides of brandy mint, lavender, and anise were used. After their 20-day application the health condition of the flight controllers improved. By the end of the working hours they felt less tired. Besides, as shown by the rheoencephalographic data, their cerebral circulation showed no abnormalities. The examinations carried out at the end of the first shift and at a high occupational load, when no phytoncides were used, showed that the REG-wave amplitude decreased and tonic tension of cerebral vessels (α, α/T, α/β) increased; these changes are typical of fatigue. When the biologically active substances were employed, the changes were of the opposite pattern: adequately increased mental capacity, reactions which included a diminished tension of the vascular wall and a moderately increased blood content of the vessels.

[Text] In the complex man-machine-environment system of interaction, improvement of operator reliability and prevention of fatigue are determined to a significant extent by improved ambient cinditions. This problem is particularly important with reference to air traffic controllers (ATC), whose work is one of the most intense and responsible types of operator work.

Use of volatile, biologically active substances (BAS), which are discharged by higher plants, is quite promising for improvement of working conditions (particularly in confined rooms). Combined investigation of the biological properties of these substances made it possible to select combinations that have a wide spectrum of antibacterial and antifungal action, in particular, with reference to pathogenic and conditionally pathogenic microorganisms [1], which are instrumental in enhancing systemic reactivity [2], improving the functional state of the cardiovascular system and psychological functions [3-5].

In view of the distinctions of ATC work, which involves great mental tension, we used the results of examining the effects of phytoncides [substances with

combination of bactericidal, fungicidal and protozoacidal properties] on dynamics of cerebral circulation in a study of their efficacy. It is known that there is a close link between functional activity of different parts of the brain and intensity of delivery of blood to them.

We used a simple method of rheoencephalography (REG), which enabled us to obtain quantitative characteristics of intensity of blood delivery, elasticity and tonus of cerebral vessels, as well as efflux of blood from the brain over the venous system [6-8].

Methods

Studies were conducted at the automated civil aviation air traffic control station (closed premises, equipped with air-conditioning system) of 41 controllers 21 to 42 years of age (average 27 years). The used combination of essential oils of lavender, peppermint and anise, which are known for their curative properties, had a pleasant fragrance and refreshing effect. The phytoncides were added to the air by means of a special batcher in the form of aerosols to the level of natural concentrations (about 1.0 mg/m^3) once per shift for 20 min.

The studies were pursued during the day and evening shifts, at the beginning and end of the shifts: 1st series--before use of BAS (background), 2d series--after 10 days and 3d--after 20 days of regular use of BAS. In all, 134 tests were made.

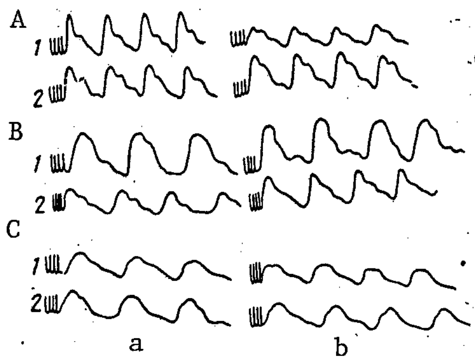
The REG was recorded on the subjects in seated position, symmetrically from both hemispheres in the frontomastoid lead, which characterizes circulation in the reservoir of the internal carotid artery. The recording was made with breath-holding in expiration. Synchronously with the REG, we also recorded the differential curve of the EKG.

To assess the REG, we used qualitative and quantitative analytical methods. We used the most informative amplitude and time characteristics: amplitude of REG expressed by the rheographic index (RI), coefficient of asymmetry (CA), dicrotic index (DCI), diastolic index (DSI), duration of anacrotic phase α, duration of catacrotic phase β and of the entire REG wave T, time of propagation of REG wave and Q-a, α/T and α/β (%).

Results and Discussion

In the background study, most controllers' REG was characterized by a steep elevation of the anacrotic phase, pointed or slightly rounded peak, slow descent of catacrotic phase and distinct dicrotic wave in its middle third, which corresponds to the criteria for normal shape according to the literature (see Figure, A).

However, we were impressed by the relatively frequent change in form of REG, in spite of the young age of the controllers, with appearance of a flattened, hump-like or plateau-like peak and dicrotic wave, sometimes smoothed, rising toward it (in 34% of the cases, see Figure, B). Such REG's resembled the changes described under emotional stress [9-12], as well as at the early



REG of controllers 23 (A), 28 (B) and 42 (C) years of age during work (left hemisphere)

1) background study
2) after 20 days of using phytoncides

a) beginning of shift
b) end (first shift)

stages of essential hypertension, particularly forms with a systolic or dicrotic wave rising above the main one [7, 3]. In one controller (42 years old), the shape of the curve corresponded to changes in the presence of atherosclerosis (see Figure, C).

The quantitative parameters also fluctuated within the physiological range on both shifts in most controllers. However, it is important to mention the appreciable extension of α to 0.167-0.242 s in 6 people (19% of the cases, mainly 29-42 years of age), which reflected increase in tonus of cerebral vessels.

At the end of the work day, the dynamics of REG parameters differed in direction in subjects working on the two shifts. It should be noted that their work loads also differed. The work load was greatest at 1200-1800 hours. For this reason, this parameter was higher at the end of the work day in subjects working the first shift and lower than at the start of the shift for those working on the second shift.

The background study made at the end of the shift of controllers working on the first shift revealed reliable decrease in REG amplitude, drop of RI on the average from 1.99±0.148 to 1.84±0.122 (-7.5%, P = 0.05; see Figure, A), which was associated with extension of anacrotic phase, from 0.125±0.0101 to 1.130±0.0106 s (+3.6%; P = 0.01), increase in coefficient α/T from 14.2±0.77 to 15.3±0.76% (+7.7%; P = 0.65) and α/β from 18.8±1.84 to 20.3±1.55% (+8%; P = 0.05), which was indicative of increased tonus of cerebral vessels and diminished intensity of delivery of blood to them. DCI dropped from 67.2±3.65 to 60.9±3.25% (-9.3%; P = 0.05).

In controllers who worked on the second shift, who had a smaller work load, there was an increase in RI at the end of the shift from 1.95±0.125 to 2.12±0.130 (+8.5%, P = 0.05) without significant change in vascular tonus. There was no reliable change in other parameters.

The increased tonus of cerebral vessels and, at the same time, decreased delivery of blood to them at the end of the first shift when there is the maximum work load can hardly be considered an adequate state of neurodynamics and hemodynamics during intensive mental work. According to data in the literature, an increase in mental work load is associated with increase in REG amplitude and decrease in tonus, i.e., active dilatation of vessels [9, 10, 14, 15]. In the case of prolonged mental work and developed fatigue, there is manifestation of increased cerebrovascular tonus and decrease in delivery of blood [14, 16, 17].

With regular use of phytoncides, half the subjects felt better, experienced less fatigue, heavy-headed feeling, unpleasant sensations in the eyes at the end of the shift, and their sleep also improved. At the same time, positive dynamics of REG parameters were demonstrable. The hypertensive types of REG, which were probably related to emotional tension (see Figure, 2B) in the young controllers (5 people), changed to the normotonic type, but persisted in half the subjects 29-42 years of age (6 people), in whom there were apparently more marked tonic or structural-tonic changes in the walls of cerebral vessels (see Figure, 2C).

There was a decline of parameters of tonus of vascular walls, as compared to background values, which was more marked after using BAS for 20 days than for 10 days. Thus, in individuals who worked on the second shift, there was significant shortening of the anacrotic phase at the start (α = 7.5%; $P<0.05$) and end of the work period (-12.6%; $P = 0.01$). with decrease in parameters α/T (-14.3%, $P = 0.01$ and -16.3%, $P = 0.05$, respectively) and α/β (-17.3%, $P = 0.05$ and -14.8%, $P = 0.05$), decline of diastolic index (DSI -7.8%, $P = 0.01$ and -10.7%, $P<0.05$), which was indicative of improved venous efflux of blood.

There was manifestation of reliable dynamics of decline of indicators of vascular tonus after 20 days of using BAS, not only in comparison to background values, but to data after 10-day use of phytoncides.

There was distinct manifestation of the beneficial effect of BAS on vascular reactivity in the course of the work day. After using BAS for 10 days, the individuals on the first shift still showed a tendency toward decline of REG amplitude by the end of the work day, as was the case in the background; in controllers working the second shift there was a tendency toward increase in amplitude. At the same time, even after 10 days of using BAS, the subjects showed a decline of parameters of tonic tension of vascular walls at the end of the first shift, as compared to its start (α -1.3%, $P = 0.05$; α/T -8.4%, $P = 0.05$; and α/β -9.4%, $P = 0.05$). There was also an extension of total REG time (T +9.0%, $P<0.05$).

After using BAS for 20 days, the first shift of controllers showed a reliable increase of RI at the end of the work day from 1.80 ± 0.109 to an average of 1.96 ± 0.111 (+8.9%, $P = 0.05$), as compared to the start of the work day, unlike the data for the background study, and a corresponding shortening of the anacrotic phase (-1.3%, $P<0.05$). There was also an increase in the period of propagation of the REG wave (Q-a +0.7%; $P = 0.01$), which was indicative of reduction of elastic properties of the walls of large vessels.

In subjects who worked on the second shift, RI did not change appreciably at the end of the work period, when the work load was smaller than at the start; however, the anacrotic phase was shorter (-3.9%, $P<0.05$).

The differences in dynamics of the main REG parameters during work on both shifts can be attributed to the dissimilar work loads and, in part, circadian rhythm of physiological functions.

The REG dynamics indicated a reduction of tonic tension of arterial walls under the effect of BAS, whereas with concurrent increase in RI in individuals

working on the first shift, at the end of the work day, unlike the background values, the dynamics characterized an adequate vascular reaction aimed at a moderate increase in delivery of blood to the brain during intense mental work. Such dynamics reflected the less marked strain on regulatory mechanisms and increase in adaptive capacities of the body in the course of work.

The prevalent tendency toward decrease in tonus of cerebral vessels, i.e., its normalization, merits special attention with regard to the effects of the BAS combination we used, and this could be utilized for preventing vascular disorders in operators whose work involves chronic nervous and emotional stress.

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EXPERIMENTAL APPROACH TO VALIDATION OF A COMBINED SANITATION METHOD FOR COSMONAUTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 6 Jul 82) pp 83-86

[Article by S. N. Zaloguyev, A. N. Viktorov, V. Ya. Prokhorov, K. R. Tolovskaya, I. A. Parchinskaya, V. P. Gorshkov, K. V. Zarubina, M. M. Shinkareva and T. Yu. Norkina]

[Text] It was previously shown [1] that one of the probable sources of infection during a spaceflight could be healthy individuals as crew members who are carriers of Staphylococcus aureus on the mucosa of their upper respiratory tract.

Development of effective methods of disinfecting healthy carriers of conditionally pathogenic microorganisms is a pressing problem for public health also.

Efforts made by various authors [2-5] to obtain the necessary result with respect to assanation by local application of various antimicrobial agents yielded rather limited and brief effects. The desired result was not achieved in cases where the carriers of pathogenic staphylococci were submitted to specific immunization with staphylococcal toxoid [2].

On the basis of clinical experience and current conceptions of the pathogenesis of St. aureus carrier state in health subjects [3-5], studies were pursued to explore the possibility of creating the necessary conditions to eliminate pathogenic staphylococci from carriers by means of a combined treatment, which included agents for direct suppression of the existing microbial focus against the background of stimulating the immunity system.

Methods

For our studies, we selected a group of healthy men (6 people) 30 to 40 years of age, who were consistent carriers of St. aureus on the mucosa of the upper respiratory tract according to numerous (at least 3) microbiological tests. The subjects underwent assanation twice (at a 1-year interval) over a period of 2.5 years. The treatment course consisted of administration of immunogenic antistaphylococcal agents, which were developed in the Laboratory of Staphylococcal Infections at the Institute of Epidemiology and Microbiology

imeni N. F. Gamalyea, and application of antiseptics (furacillin 1:5000, 1-1.5% peroxide) to the mucosa of the nose, mouth and throat, followed by application of polyvalent therapeutic staphylococcal bacteriophage in the form of solutions and ointments.

After the second course of disinfectant measures, some of the subjects (3 men) spent 45 days in a sealed chamber where some of the features inherent in a spacecraft cabin were simulated (chemical composition of air, ionization background, diet, sanitary and hygienic facilities).

Over a period of 2.5 years, we examined many times the quantitative parameters and species composition of microflora of the nose, as well as mouth and throat of the subjects. Specimens were cultivated on the surface of 5% Hottinger blood agar, mannitol-salt agar, bromthymol blue agar (for isolation of Gram-negative bacteria) and Sabouraud agar. The microorganisms were identified in accordance with the Bergey manual [6]. Staphylococcal cultures were identified as the St. aureus species according to their capacity to decompose mannitol under anaerobic conditions, produce coagulase, lecithinase and α-toxin. St. aureus strains were submitted to phage typing with the international set of staphylococcal bacteriophages; we tested their sensitivity to antibiotics. G. O. Pozharskiy selected the microbiological samples and administered antibacterials to the subjects.

Results and Discussion

After the first course of sanitizing measures, positive changes were noted in the staphylococcal flora of the subjects (Tables 1 and 2): in some cases there was complete elimination of St. aureus from various biotopes in the carriers, replacement of the original cultures with strains with lower toxigenic activity (1:1280 titer of α-toxin in the initial cultures and 1:320-1:10 in the ones that appeared in their place), which had a broader range of antibiotic sensitivity. These beneficial changes persisted for a long time, up to 6 months. A recheck after this period to assess specific immunity was indicative of presence of rather high antitoxic protection in the subjects. The titers of anti-α-toxin in blood serum constituted 1-5 AU [antitoxin units] (in the background period these parameters did not exceed 1 AU).

The positive effect of the instituted measures was also confirmed by the results of tests of nonspecific immunity and allergological status of the subjects, which were performed by S. I. Pal'mina and I. V. Konstantinova et al. Such parameters as phagocytic activity of blood neutrophils, levels of secretory and serum immunoglobulins were on high levels after treatment. In addition, there was disappearance of signs of sensitization to staphylococci, which were demonstrable by the leukocyte migration inhibition test, as well as blast transformation method. What is also important is the fact that there were beneficial changes in the species composition of autoflora of subjects who were treated, as manifested by elimination of microorganisms that are not inherent in the tested mucosal regions (Candida sp., enterococci, enterobacteria), which had been demonstrated in the background period in these subjects.

Table 1. Dynamics of Staph. aureus content in upper respiratory tract of subjects in the usual environment (quantity of cells per tampon for the nasal cavity, quantity of cells per 5 mℓ washings for the mouth and throat)

SUBJECT	LOCALIZATION OF MICROBIAL FOCUS	TESTING TIME: BEFORE SANITATION MEASURES	ONE MONTH AFTER FIRST COURSE OF SANITATION	SIX MONTHS AFTER FIRST COURSE OF SANITATION	IMMEDIATELY AFTER SECOND COURSE OF SANITATION	ONE MONTH AFTER SECOND COURSE OF SANITATION
ZH-KO	NOSE	10^2—10^6 (80)	NONE FOUND	NONE	NONE	NONE
	MOUTH AND THROAT	10^3—10^4 (80)	10^2 (29)	10^3 (H T)	NONE	NONE
P-OV	NOSE	10^4—10^5 (53/83A)	10^4 (53/83A)	10^4 (53/83A)	2×10^1 (H/T)	NONE
	MOUTH AND THROAT	10^2—10^3 (53/83A)	10^3 (3A/3C)	10^2 (53/83A)	NONE	NONE
TS-OV	NOSE	10^3 (85)	10^2 (H/T)	10^2 (H/T)	NONE	NONE
	MOUTH AND THROAT	10^2—10^3 (85)	10^3 (H/T)	NONE	NONE	10^2 (42E/75)

Note: Here and in Table 2, the phagotype is given in parentheses.
[H/T--expansion unknown]

Table 2. Dynamics of Staph. aureus content in subjects' upper respiratory tract during stay in sealed chamber (quantity of cells per tampon for the nasal cavity, quantity of cells per 5 mℓ washings for the mouth and throat)

SUBJECT	LOCALIZATION OF MICROBIAL FOCUS	TESTING TIME: BEFORE SANITATION MEASURES	ONE MONTH AFTER FIRST COURSE OF SANITATION	SIX MONTHS AFTER FIRST COURSE OF SANITATION	IMMEDIATELY AFTER SECOND COURSE OF SANITATION	ONE MONTH AFTER SECOND COURSE OF SANITATION
M-OV	NOSE	10^2—10^4 (80)	10^3 (80)	10^4 (H/T)	10^2 (H/T, 3C/55/71)	10^3 (H/T, 3C/55/71)
	MOUTH AND THROAT	10^2—10^3 (80)	10^3 (80)	10^2 (H/T)	10^2 (H/T)	10^2 (H/T)
ZH-EV	NOSE	10^5—10^6 (29)	10^5 (29)	10^5 (29)	10^4 (29)	10^3 (29)
	MOUTH AND THROAT	10^2—10^4 (29)	10^3 (29)	NONE	10^3 (29, 3C/55/71)	10^4 (29)
P-IY	NOSE	10^4 (H/T)	NONE	NONE	NONE	NONE
	MOUTH AND THROAT	10^3—10^5 (3C/55/71)	10^5 (3C/55/71)	10^5 (3C/55/71)	10^4 (3C/55/71)	10^3 (3C/55/71)

One month after the second course of sanitizing measures, pathogenic staphylococci were demonstrated once in a negligible quantity in only one of the subjects (Ts-ov), in his mouth, in the group of subjects who were in their usual environment. These cultures, which were referable to phagotype 42E/75, had never before been detected in him at numerous prior tests.

According to our set goals, it was particularly important to assess the effect of sanitizing treatment on healthy St. aureus carriers who spent time in a sealed chamber.

The data accumulated to date [1, 5, 7] indicate that, under hypokinetic conditions, during stays in pressurized cabins, as well as during spaceflights, individuals who are carriers of pathogenic staphylococci show enlargement of the microbial focus of St. aureus, increase in virulence of vegetating cultures, increase in number of strains with multiple resistance to antibiotics. As an example, we can describe the results of our own studies: while in the usual environment, constant St. aureus carriers showed $2 \cdot 10^2$–10^3 cells/sponge of these microorganisms in the nose, when they spent time in a sealed chamber, as well as spacecraft cabins, it increased to $3 \cdot 10^3$–10^5 and $2 \cdot 10^4$–$2 \cdot 10^6$ microorganisms, respectively.

In contrast, no adverse changes in the staphylococcal flora were demonstrated in subjects who had undergone combined pretreatment in the course of a long stay (over 1 month) in a sealed chamber. The size of the foci that were formed on their mucous membranes did not increase, whereas in two subjects (M-ov and Zh-ev) there was a distinct tendency toward decrease in pathogenic staphylococci in the main biotopes. The toxigenic activity of St. aureus strains persisted at a low level in the course of the study and there was no breeding of cultures with multiple antibiotic resistance.

Thus, the results of our studies are indicative of the suitability and efficacy of the proposed combined method of sanitizing healthy carriers of St. aureus, under both ordinary living conditions and during stays in sealed, confined spaces.

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METHODS

UDC: 629.78:613.165

PREDICTION AND IDENTIFICATION OF COSMIC SOLAR RADIATION FLUX AND SPECTRA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 14 May 82) pp 86-89

[Article by S. I. Avdyushin, N. K. Pereyaslova, P. M. Svidskiy and A. B. Malyshev]

[Text] As a result of investigating the link between characteristics of cosmic solar radiation (CSR) events and parameters of heliogeophysical phenomena that accompany a solar burst, several patterns were established, which served as the basis of forecasting methods. The method of concurrent examination of the set of heliogeophysical phenomena associated with a solar burst is used to solve forecasting problems.

The data about solar activity, flux of penetrating radiation in the interplanetary environment and magnetosphere, as well as about the state of the interplanetary environment, which are needed for analysis, are provided by cosmic, stratospheric and ground-based equipment, which forms a regulation observation network of the radiation situation service (RSS).

At the present time, a method has been developed and is used in RSS practice of forecasting development of CSR fluxes and integral flux over an entire event, which makes use of a model of isotropic diffusion and data from initial recording in polar zones of CSR fluxes on the Meteor satellite [1]. For tentative calculation of proton flux, a linear function is used:

$$\ln\left(I \cdot T^{\frac{3}{2-\beta}}\right) = -a\,\frac{1}{T} + b,$$

which was obtained from the diffusion equation, where I is proton flux density determined from a special program of ongoing monitoring of CSR fluxes and galactic cosmic radiation, which was developed for the Minsk-32 digital computer; $T = t_{meas} - t_0$, where t_{meas} is the time of measurement of flux density in polar zones and t_0 is the moment that protons exit from the burst region, which is determined on the basis of data about heliogeophysical phenomena that are regularly [operationally] transmitted to the RSS. Injection time can be determined from x- or radiowave radiation accompanying the proton burst and from optical observations in H_α. Preference is given to the time

hard x-radiation surge [flash-up]. If such data are not available, the start of observation of burst in H_α is taken as t_0. In the case of recording flux from retrolimbal bursts, the time of observation of the radiowave radiation surge is taken as t_0 (II, IV type).

Identification of current status of radiation situation over the flight course of space vehicles in near-earth orbits involves the change from observing fluxes of penetrating radiation in the orbit of the Meteor artificial earth satellite in the high-latitude zones of earth's magnetosphere to a description of general structure of particle flux, in particular on orbits of the Salyut-Soyuz manned spacecraft (MSC). This transition must be made primarily for CSR protons with consideration of actual thresholds of geomagnetic hardness, which depends on the degree of disturbance of the magnetosphere. The change to a specified course is based on the observed energy spectrum of SCR particles at the polar caps, characteristics of spatial distribution of cut-off hardness and current orbital parameters.

Since the state of the magnetosphere can change appreciable in time, one needs a dynamic model of threshold hardness to solve transition problems. Such a model is written in analytical form as an expression that relates hardness to McIlwein's parameter L:

$$R = \frac{15}{L^{2+\delta}}\left[1-\left(\frac{L-1}{L_0-1}\right)^3\right]^{1,4}$$

for $L<L_0$; $R = 0$ for $L \geqslant L_0$. Parameters δ and L_0 take into consideration the main features of the magnetosphere: L_0 limit of polar cap in the night sector of the magnetosphere; δ is quantitatively linked to D_{st} variation, which reflects the intensity of ring [circular] current [2]. Under calm conditions $L_0 = 7$, or $\approx 68°$ invariant latitude, $\delta = 0$. As a result of comparing observations of CSR protons to the value of D_{st} variation, an empirical function was established.

A pattern that consists of regular shift of the arm [limb?] of the latitudinal course of cosmic rays with increase in intensity of ring current, which is determined from observations aboard the Meteor, is the basis for determining the value of D_{st} variation. Quantitatively, this link can be described by the expression $\Delta L = (L_H - 1) \cdot 10^{-2} (D_{st})^{2/3}$, where ΔL is the shift of the arm from the calm level and L_H is a calm arm level in undisturbed magnetosphere.

It is important to note that the basic ongoing parameters (energy spectrum of particles and characteristics of distribution of threshold geomagnetic hardness) are obtained simultaneously from readings aboard the Meteor. Using this model, a working classification ["catalogue"] of integral CSR proton spectra was calculated for a set of orbits of Salyut-Soyuz MSC for different initial spectra of protons in polar caps and state of magnetosphere, which is characterized by parameters δ and L_0 of the model of threshold geomagnetic hardness.

The results of studies pursued in recent years revealed that photospheric magnetic fields are a significant factor, which determines the distribution

of protons generated in a brust. This was established for the first time in the analysis of experimental data obtained on Mariner-2. Subsequently [3], a comparison was drawn between the nature of changes in CSR profiles with E_p>1 MeV in interplanetary space as a function of coronal structure of the sun's magnetic field, and it was found that low-energy solar protons fill unipolar magneitc regions in the corona, and the interfaces of magnetic polarities serve as a considerable obstacle to their longitudinal distribution. We analyzed the observed characteristics of solar protons with energy of 5 to 40 MeV, which were recorded on the Meteor with the configuration of large-scale magnetic fields on the sun for periods of maximum and decline in the 20th cycle of solar activity, as well as at the build-up stage of the 21st cycle. We used maps of solar magnetic fields, the method of plotting which is described by McIntosh [4]. Taking into consideration the demonstrated distinctions of distribution of CSR protons [5-7], a method was developed that enabled us to forecast the following parameters of proton events: constants of decline of proton flux with energy E_p>5 MeV: T_1--from maximum intensity I_{max} to $I_{max}/2$ and T_2--from maximum to intensity at the boundary of the unipolar region; time of maximum intensity of CSR with E_p>5 MeV: t_1 and t_2--in events where longitude of connection and burst were in the same and different unipolar regions, respectively; complete flux of protons with E_p>5-10 MeV and E_p>40-60 MeV, normalized to maximum intensity, log $I/I_{max}3600$; beginning and duration of event; parameters of hardness of integral spectra at maximum intensity γ_{max} and at the start of the event on the level of the half-maximum γ_{start}.

Reliability of prediction of parameters

PARAMETER	PROTON ENERGY, MEV	RELIABIL. OF ESTIMATE		COEFFICIENT OF CORRELATION	RELATIVE ERROR, %
		$\alpha = 0,90$	$\alpha = 0,95$		
T_1, H	>5	6	8	0,95	45
T_2, H	>5	7	9	0,90	45
t_1	>5—10	7	8	0,80	70
t_2	>5	3	4	0,87	30
TOTAL FLUX	>5—10	0,2	0,3	0,89	50
	>40—60	0,3	0,4	0,78	50
γ_{ST}	>10—30	1,0	1,1	0,78	90
	>30—60	0,7	0,8	0,94	90
γ_{max}	>10—30	0,9	1,0	0,79	80
	>30—60	0,7	0,8	0,94	80

The Table lists the coefficients of correlation and relative error of forecast parameters for all those determined by the parameter method.

The block diagram of the forecast of parameters of CSR events is illustrated. Figure 1 shows an example of an "epignosis" [?] of proton flux in the CSR even of 17-20 September 1977.

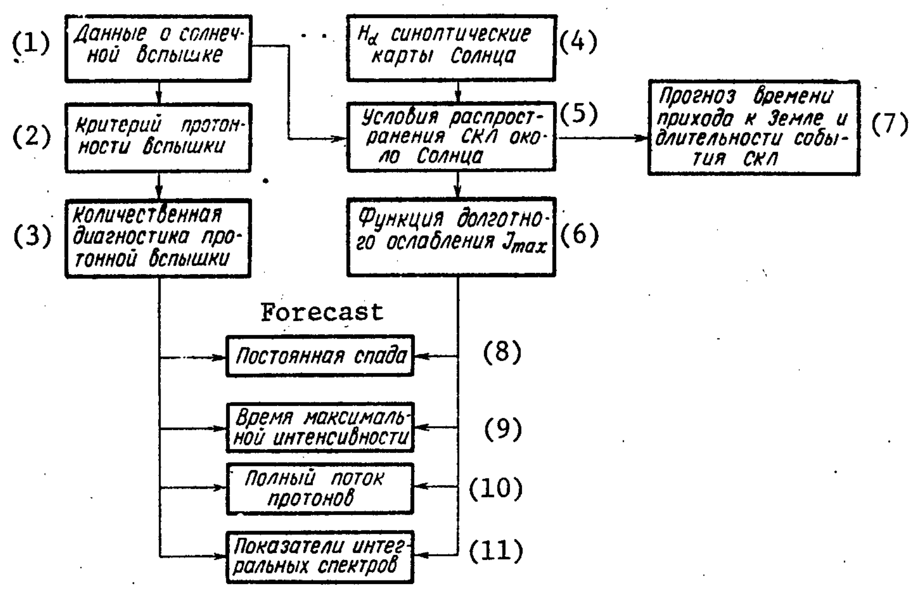
Studies of characteristics of micro-wave surges of radiowave radiation and their relation to proton flux in CSR events as a function of conditions in the radiating regions and helio longitude of injection source, patterns were obtained that were used to develop forecasting methods [8-12].

According to radio observations in the centimeter range, methods were developed for predicting the parameters of proton events:

1. Estimate of probability of recording protons with E_p>60 MeV according to observations at frequencies of 8800 and 4995 MHz.

The following parameters were used: I_r--flux of radiowave radiation at maximum; I_r--integral flux for entire event, defined as $I = I_r d$, where d is effective duration.

Block diagram of forecast of proton events



Key:
1) data about solar burst
2) criterion of proton content of burst
3) quantitative identification of proton burst
4) H_α synoptic maps of sun
5) conditions for dissemination of CSR near sun
6) function of longitudinal attenuation of I_{max}
7) prediction of time of arrival on earth and duration of CSR event
8) decline constant
9) time of maximum intensity
10) complete proton flow
11) parameters of integral spectra

2. Forecast of bottom limit of proton flux with E_p>10 MeV at event maximum according to observations at ν = 9100 MHz.

The bottom range of proton flux with E_p>10 MeV for 0.84, 0.89 and 0.92 probability of correct forecast is determined with consideration of helio-longitudinal attenuation of intensity of the radiowave surge by means of introducing coefficient $K_r(\phi)$ from the following equations:

$$\lg I_p^{max} = \begin{array}{l} 1{,}279\,\{\lg I_r^{max} - 2{,}26K_r(\varphi)\} - 1{,}36 \\ 1{,}279\,\{\lg I_r^{max} - 2{,}26K_r(\varphi)\} - 1{,}45 \\ 1{,}279\,\{\lg I_r^{max} - 2{,}26K_r(\varphi)\} - 1{,}54 \end{array}$$

The data required for the forecast can be obtained from the Zimenka (USSR) station, where two identical radiotelescopes are used for monitoring ["patrol"] at 9100 MHz.

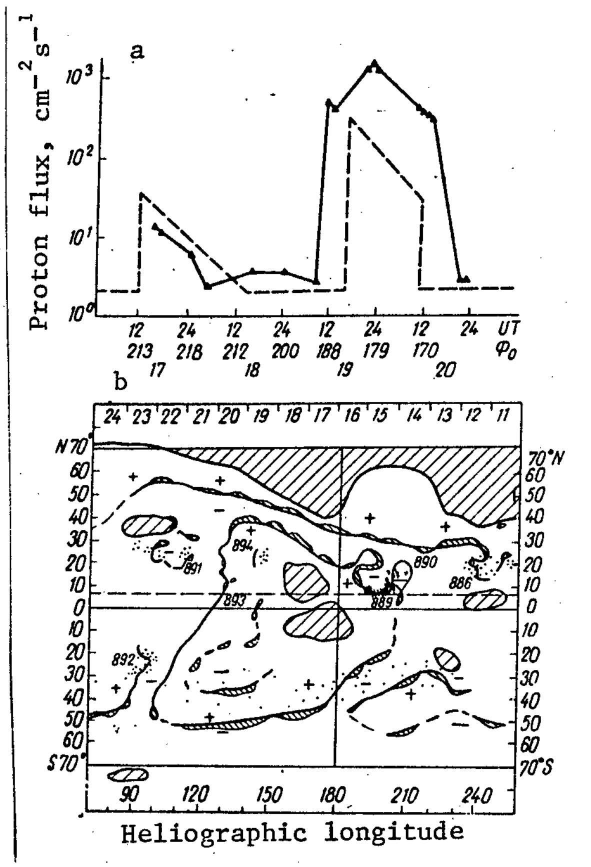


Figure 1.
Epignosis of time distribution of CSR with E_p>15 MeV in the event of 17-20 September 1977 (a) and synoptic map of sun (b)

Black triangles refer to experimentally measured proton flux; dash line is predicted magnitude of proton flux

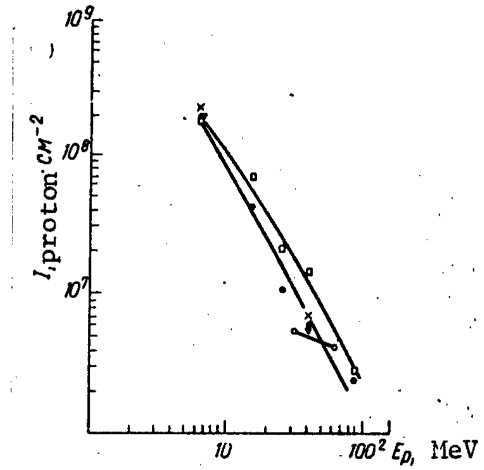


Figure 2.
Measured and predicted integral proton flux for entire event (30 April 1976) as a function of threshold energy

Here and in Figure 3: black circles refer to measured complete flux, squares--predicted proton flux according to Krimigis model; x--the same according to combined model; white circles--same according to data about radio surges and triangle--same according to Lupton-Stone model

3. High-speed forecast of integral proton flux over entire event.

Integral proton flux I_p was calculated on the basis of data about flux at maximum of event for protons with E_p>30 and 60 MeV and time before maximum according to formula in [13]:

where $\tau = \frac{t_m}{t_0}$, I_{max} is proton flux at maximum, t_m is time before maximum, θ is a Heaviside function, α, β and t_0 are numerical constants.

Accuracy of flux forecasting constituted at least 20-30%. The data for the forecasts were received from the Meteor satellite.

X-radiation is a highly informative predictor-parameter of "proton content" of a burst. With regular receipt of data in the x-radiation range of 0.5-4 and 1-8 Å, one can calculate the integral flux in CSR events before the protons

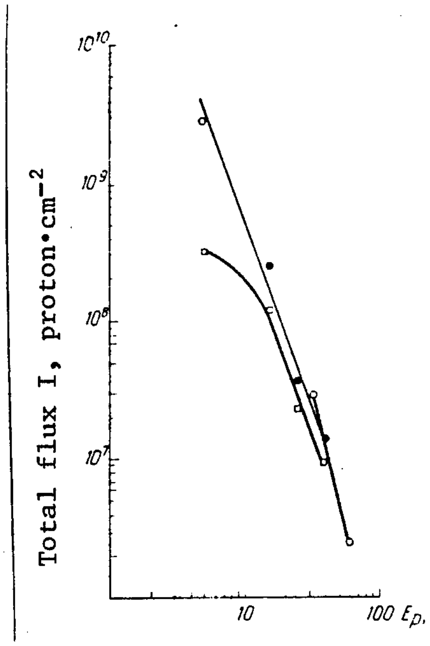


Figure 3. Measured easured and predicted integral proton flux over entire event (13 Feb 1978) as a function of threshold energy

come into earth's orbit, i.e., the time up to accumulation of maximum dose. Regression analysis is used to predict in stages the radiation characteristics of CSR events: radiation dosage and hardness of spectrum [15, 16]. The developed forecasting methods were used to predict integral fluxes in the CSR events of 30 April 1976 and 13 February 1978. Figures 2 and 3 illustrate the experimentally measured and predicted integral proton flux for the entire event as a function of threshold energy. The forecasts were made according to the models of Krimigis [13], Lupton-Stone [14], combined model that takes into consideration coronal distribution and subsequent migration of protons along the force lines in interplanetary space and the method that makes use of characteristics of radiowave radiation which accompanies bursts. The accuracy of forecast I_p is substantially related to threshold energy and the model used. Hence, in forecasting the parameters of the radiation situation one must take into consideration the distinctions of yield and distribution of particles in interplanetary space for each concrete CSR event. There should be further investigations of the forecasting methods that have been developed and their applicability to events in the 21st cycle of solar activity.

A method based on the results of statistical analysis of information about the characteristics of solar proton flux can be used for long-term forecasting. The distinction of this method is that it involves separate analysis of the times of appearance of proton bursts and magnitude of proton flux in each burst. As a result of such analysis, determination is made of the patterns and distribution of these parameters and the correlation is found to determine the combined probability of appearance of events.

Global automated dynamic models of the radiation situation are recommended for development and refinement of work dealing with direct identification and forecasting.

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UDC: 629.78:612.82

STUDY OF PSYCHOPHYSIOLOGICAL DISTINCTIONS OF PRIMATES USING DELAYED REACTION TEST

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 22 Apr 82) pp 90-92

[Article by I. P. Sheremet, G. S. Belkaniya and N. F. Sofiadis]

[Text] The efficacy of teaching and training is largely determined by the characteristics of animals' higher nervous activity (HNA). Such elements of HNA as short-term and long-term memory, which correlate the most with the learning capacity of animals, are particularly important.

In view of the need to screen monkeys for teaching them operator work following the program of preparations for an experiment aboard an artificial earth satellite, our aim was to search for and refine an objective psychophysiological test. The method of testing delayed reactions (DR), which is used extensively to assess intercentral relations in the CNS [central nervous system], effect of diverse factors on human and animal memory [1-3] and experimental study of interaction between different forms of memory [3-6] served as our basis.

DR are a complex neuropsychological phenomenon and for this reason most studies deal with the reflex basis and neurophysiology of DR. Our purpose here was to adapt the method of testing DR to the test requirements, as well as to use the developed DR test to evaluate individual psychophysiological reactivity of monkeys.

Methods

The studies were pursued with 44 Macaca rhesus males 20-36 months of age. The test was performed on a fasting stomach and 2 days after placing animals in a primatological chair. We used the direct version of the method of testing DR with presentation of a special test feeder. The latter consisted of a piece of wood 30×8×3 cm in size with three wells 6 cm apart, and the wells were 5 cm in diameter. Each well was covered with a lid that was attached to a sliding bolt at one of the edges, so that it could be readily moved aside. In plain view of the animals, the bait was put in one of the wells and covered with the lid. After a certain time, which equaled the delay, the test feeder was presented to the animal. The bait was placed in different wells at random (using tables of random numbers).

We conducted the DR test for 4 days. Zero day (preparatory), when the animals became familiar with the manipulations on the test feeder, directly preceded the test. For the first 3 days [1-3], the delay was constant and constituted 5 s, with 15 presentations. On the 4th day [4], we used a variable delay of 5, 10, 40, 80 and 120 s, with 8 presentations for each delay time. During the tests, we recorded accuracy of animals' responses, functional asymmetry (dextromanual or sinistromanual), reaction time (between time of presentation of test feeder and taking bait), before and after the DR test we measured blood pressure. Physical development of animals (muscular and bone components) was assessed using a method developed at the Institute of Anthropology, Moscow State University [7].

Results and Discussion

In the tested groups of monkeys there was distinct functional asymmetry, which was manifested by preference for using the right or left hand for the test. The literature on this score is contradictory. For example, Lehman [8] states that no distinct preference in use of hands is demonstrable in primates, and at the same time it is noted that, already upon the first presentation, one can predict with a high degree of probability the hand preference in the next 600 presentations. Several works indicate that there is no morphological or functional asymmetry of the cerebral hemispheres in primates [9, 10]; however, a consistent preference is observed after surgical disruption of hemisphere symmetry [9].

In our study, we took the percentile ratio of preference for using the right or left hand to get feed from the well to the total number of presentations on each experimental day and to all presentations for the 4 days of the test as an indicator of functional asymmetry. The differences between parameters of functional asymmetry were considered significant with $P<0.05$.

The results of our analysis revealed that, out of the 44 rhesus monkeys, 20% preferred to use their left hand, 64% their right hand and 16% used both hands to perform the test. Hand preference is strongly related to parameters of physical development of the preferred limb ($r\approx0.5$; $P<0.01$), which is indicative of correspondence between functional and somatic asymmetry and a high probability that these properties will coincide in rhesus monkeys. It should be noted that some of the monkeys in the group under study subsequently underwent operator training in a special simulator, in which the hand lever was to the left of the animal. Upon repeating the DR test, animals who had fully learned the program for manual operator work initially showed no change in hand preference. This is indicative, on the one hand, of stability of asymmetry and, on the other hand, of functional flexibility in learning. Nevertheless, we believe that our findings should be taken into consideration in designing training equipment and screening animals.

We used the following as the main parameters of psychophysiological reactivity of monkeys according to the DR test:

PR--level of positive responses, as percentage of all presentations on different test days [1-4] and with variable delays (5, 10, 40, 80, 120 s).

$\overline{X}_{PR}$--mean level of responses for all days of test with 5-s delay (total of 53 presentations).

ΔPR_{4-1}--difference in PR between 4th and 1st test days, which makes it possible to take into consideration the direction (+, 0, -) of learning dynamics.

$\overline{X}_{RT}$--average reaction time on different days, with variable delays and for all test days with 5-s delay

$\overline{X}_{PR}/\overline{X}_{RT}$--ratio of average level of responses on test days to average reaction time: an increase of this parameter is interpreted as a positive characteristic of psychophysiological reactivity and a decrease, as a negative one.

Characteristics of types of psychophysiological reactivity of monkeys according to main parameters of DR test

DR test parameter	Type of psychophysiological reactivity		
	I	II	III
PR (%) with const. delay of 5 s:			
1st day	52	51	76
2d "	55	64	60
3d "	62	75	58
4th "	57	87	61
ΔPR_{4-1}	57	69	61
PR (%) with variable delay, s:	+5	+36	—26
5	57	87	50
10	53	71	50
40	36	43	42
80	35	33	17
120	32	34	17
$\overline{X}_{RT}$ (s) with const. delay of 5 s:			
1st day	3,16	3,48	4,43
2d "	2,53	2,21	3,13
3d "	2,4	2,34	2,23
4th "	2,01	2,36	2,12
For all presentations	2,53	2,60	2,98
$\overline{X}_{RT}$ with variable delay, s:			
5	2,01	2,36	2,12
10	2,3	2,01	4,56
40	2,73	2,88	2,25
80	3,40	3,24	3,43
120	2,57	4,31	3,31
$\overline{X}_{PR}/\overline{X}_{RT}$	25,61	29,99	20,13

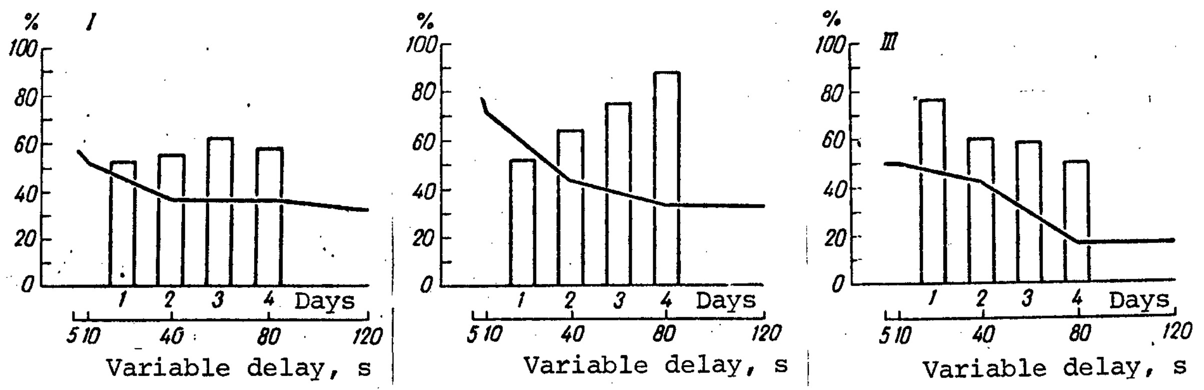
Analysis of individual indicators of psychophysiological distinctions of monkeys enabled us to single out three main groups according to the DR test, the characteristics of which were defined as psychophysiological types of rhesus monkeys (see Table and Figure). The distinction of these types was made on the basis of parameter ΔPR_{4-1}. We considered the difference between PR on the 1st and 4th days of the test to be substantial with $P<0.05$, which corresponded to a minimal difference of 20% between PR_4 and PR_1.

The second type was characterized by the same PR on all 4 test days (see Figure). $\overline{X}_{PR}$ constituted 57%, $\overline{X}_{RT}$ 2.53 s and PR/RT was 25.61. We only observed some tendency toward increase of ΔPR_{4-1} (by 5%).

The second type presented positive PR dynamics (from 51 to 87%): parameter ΔPR_{4-1} increased by 36%. $\overline{X}_{PR}$ constituted 69% and was higher than for the first type; the same applies to parameter PR/RT, which constituted 29.99. $\overline{X}_{RT}$ virtually failed to differ from type I. It should be noted that the parameters for variable delays were also highest in monkeys with psychophysiological type II.

The third type was characterized by negative PR dynamics and its parameters were considerably lower than for the first and second types (see Table). It must

be noted that it is expressly with this type of psychophysiological reactivity that there were relatively more instances of refusing to perform the test task.



Types of psychophysiological reactivity (I, II, III) in rhesus monkeys according to DR test. The bars indicate level of responses (PR) on different test days (1st-4th days), and the lines show PR with use of variable delay (5, 10, 40, 80 and 120 s)

Types I and II were the most represented (52 and 41%, respectively) in the sample we tested. Type III was demonstrated in only 7% of the monkeys.

These studies of psychophysiological distinctions of rhesus monkeys are indicative of the informativeness of the DR test that was developed. The data obtained make it possible to single out animal groups, on the basis of the DR test results, that have optimum psychophysiological characteristics for training on the program of learning operator work. Future investigations, in which we plan to compare the DR test data to parameters of learning capacity of monkeys using complex programs of operator work, will enable us to determine the degree of selective efficacy of the developed test.

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BRIEF REPORTS

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DIURNAL RHYTHM OF POTASSIUM EXCRETION IN URINE WITH MAN IN ANTIORTHOSTATIC POSITION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 10 Mar 82) pp 92-93

[Article by L. Lhagwa (Mongolian People's Republic)]

[Text] The object of this work was to analyze daily rhythm of potassium excretion in urine with man under conditions simulating the effects of weightlessness, i.e., redistribution of blood from the bottom half of the trunk to the top.

Methods

This study was conducted in January and February on 4 male subjects 23-24 years of age. To simulate weightlessness, the subjects remained supine, with the head tilted down at an angle of -8°. We assayed potassium excretion in urine by flame photometry daily, for 26 days, in each 4-h batch of urine (at 0300, 0700, 1100, 1500, 1900 and 2300 hours). In the course of analysis of the obtained data, we paid special attention to values of acrophase (maximum and minimum) at different test times and level (average of mean daytime and mean night time levels) of circadian rhythm.

Results and Discussion

There was an increase in potassium excretion in urine in the phase of the daily maximum between the 4th and 9th days of antiorthostatic position (Tables 1 and 2).

Maximum potassium excretion was referable to daytime hours. Between the 4th and 9th days, all of the subjects presented an increase in potassium excretion in the phase of the daily minimum, which coincided with night time hours.

During this period, along with increased potassium excretion at the maximum and minimum phases, there was significant increase in level of 24-h excretion (Table 3).

The increase in excretion of potassium in urine is apparently related to several factors, primarily redistribution of blood in antiorthostatic position (with excessive passage to the upper half of the body). Expressly such

Table 1. Changes in daily maximum and minimum 4-h excretion of potassium in urine in antiorthostatic position (in mg per 4 h), M±m

SUBJECT	MAXIMUM		MINIMUM	
	BACKGROUND	ANTIORTHOST.	BACKGROUND	ANTIORTHOST.
TU	435,90±4,1	766,00±4,0*	216,80±2,0	233,63±2,6*
BN	497,86±2,8	660,88±3,1*	187,13±2,7	259,29±2,1*
BR	648,72±3,3	947,88±4,6*	262,80±2,1	279,27±2,9*
EN	641,95±4,0	865,89±4,0*	213,70±3,0	215,68±2,5**

*P<0.001 **P<0.005

Table 2. Maximum and minimum excretion of potassium in urine (mg/4 h) at different periods in antiorthostatic position

DAY OF STUDY	SUBJECTS							
	TU		BN		BR		EN	
	MAX	MIN	MAX	MIN	MAX	MIN	MAX	MIN
1—3	522,92	161,00	664,12	190,25	949,93	174,23	467,67	147,08
4—6	818,67	236,50	807,45	318,67	1018,80	360,83	979,93	228,08
7—9	924,13	318,17	523,33	261,25	798,67	318,25	1219,00	270,48
10—12	798,58	218,83	648,63	267,00	1024,10	263,75	796,70	217,08

Note: Here and in Table 3 the arithmetic means are listed.

Table 3. Circadian rhythm of potassium excretion in urine (mg/4 h) at different stages of study

DAY OF STUDY	SUBJECTS			
	TU	BN	BR	EN
BACKGROUND	300,19	340,98	429,01	381,53
1—3	309,49	371,83	471,23	311,22
4—6	492,71	512,68	606,66	519,11
7—9	532,50	384,24	570,04	597,92
10—12	412,25	438,63	474,17	452,94
TOTAL ANTIORTH. PERIOD	436,91	426,84	530,52	470,32
RECOVERY PERIOD	461,51	279,41	294,02	291,72

hemodynamic changes had been observed during water immersion. In that study, increased excretion of potassium by the kidneys was already demonstrated on the 2d day of immersion; by the 7th-13th day this parameter rose even more. In addition, in antiorthostatic position there can be activation of the hypothalamo-hypophyseo-adrenal system through a mechanism of nonspecific stress reaction with increased production of corticosteroids and corresponding increase in potassium metabolism. Finally, we cannot rule out a factor, such as early stage of deconditioning, with reduction of muscle mass, which is also associated with excessive kaluresis.

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EFFECT OF SYDNOCARB AND DIHYDROERGOTAMINE ON HUMAN WORK CAPACITY DURING SIX-HOUR ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 (manuscript received 29 Sep 82) pp 93-95

[Article by O. D. Anashkin, G. V. Amel'kina and A. Yu. Modin]

[Text] At the early stage of man's adaptation to weightlessness, there is development of sensation of blood rushing to the head, spatial illusions and, in a number of cases, symptoms of motion sickness [1]. Development of symptoms of motion sickness has an appreciable effect on work capacity and operator performance of cosmonauts.

Our objective here was to assess the efficacy of a Soviet central nervous system stimulator, sydnocarb, and dihydroergotamine (DHE), which has a tonic effect on the veins, during 6-h antiorthostatic hypokinesia (AOH), on physical work capacity of man.

Methods

The studies were conducted on 8 essentially healthy men 30-39 years of age (height 171-185 cm, weight 58-85 kg). The physiological effects of weightlessness were simulated by 6-h strict bed rest with the body in antiorthostatic [head tilted down] position at -15° [2]. The subjects were in a hospital on the usual diet (3500 kcal/day). Fluid intake was not restricted.

Four series of studies were conducted, in which the same program was followed for clinical and physiological work-up. All of the subjects participated in all series of tests (at intervals of at least 14 days). In the first series, the subjects maintained the usual regimen of motor activity.

In the second series, the subjects were given placebo during 6-h AOH on the same schedule as intake of pharmacological agents used in the third and fourth series. In the third series, the subjects took sydnocarb 30 min prior to AOH (5 mg) and in the 3d and 5th hours of AOH (10 mg each time); total dosage of sydnocarb was 25 mg.

In the fourth series, the subjects took DHE of the Spofa Firm (CSSR), 2 mg at a time, 30 min before AOH, in the 3d and 9th·h of AOH, to a total dosage of 6 mg.

Effect of sydnocarb and DHE on human physical work capacity during 6-h AOH (mean parameters for 8 subjects are listed)

SERIES	AGENT	EXERCISE TIME	TOTAL WORK DONE KG-M	MAXIMUM HR/MIN	MOU L/MIN	OXYGEN UPTAKE ML/MIN/KG	OP ML/BEAT	WORK KG-M PER GRAM BODY WT.	CARDIAC FUNCTION INDEX
I	BACKGROUND	16 MIN 42 S	13 420	180,4	3002	39,1	16,7	173	360
II	PLACEBO	14 MIN 46 S	11 212	177,9	2698	35,22	15,2	145	312
		$P<0{,}05$	$P<0{,}05$		$P<0{,}01$	$P<0{,}01$	$P<0{,}01$	$P<0{,}05$	$P<0{,}05$
III	SYDNOCARB	15 MIN 38 S	12 126	181,5	2722	35,13	15,0	157	393
IV	DHE	15 MIN 44 S	12 227	176,5	2680	34,62	15,19	138	370

The physical work load was graded by means of a bicycle ergometer; the EKG was recorded continuously in the D-S lead; oxygen uptake and carbon dioxide output were recorded on an automatic Spirolit gas analyzer; arterial pressure was determined with a Medicor (Hungarian People's Republic) automatic gauge.

The subjects exercised on the bicycle ergometer in seated position, the initial load being 450 kg-m/min; it was then increased by 150 kg-m/min every 3 min as long as the subject was able to continue. Conventional clinical criteria for determining physical work capacity of man served as indications to stop the test [3, 4].

The results were processed by the method of variants related in pairs, using Student's criteria to estimate mean differences.

Results and Discussion

Before hypokinesia, all 8 subjects presented normal parameters of cardiorespiratory system reactions to maximum load for healthy man, which conforms with data in the literature [4-6].

As can be seen in the Table, after 6-h AOH, there was a reliable decline of physical work capacity, as confirmed by the decrease in maximum oxygen uptake (MOU), decrease in oxygen uptake per kg body weight and oxygen pulse (OP) by an average of 10%.

It is known that physical work capacity is determined by the level of oxygen uptake, which normally depends on degree of muscular development, cardiac output and arteriovenous difference for oxygen [7].

With intake of placebo, after 6-h AOH, 7 subjects presented a decrease by an average of 304 mℓ in MOU, while this parameter did not change in 1 subject. The reduced work time, total volume of work and cardiac function index were indicative of diminished physical work capacity.

With intake of sydnocarb, work time on the bicycle ergometer and, consequently, amount of performed work increased in 5 subjects, as compared to those who took placebo, remained at virtually the same level in 2 cases and decreased in 1. On the average, it was possible to increase somewhat work time, total volume of work and index of cardiac function in the third series, as compared to parameters with intake of placebo. MOU ($\dot{U}O_2$ in mℓ/min/kg) and OP showed virtually no difference from the average levels obtained with intake of placebo.

With use of venous tonus stimulating agent, DHE, work time and amount of work increased in 7 cases and decreased in 1 subject, as compared to intake of placebo.

With intake of DHE, there was an increase in average work time, total volume of work and index of cardiac function, as compared to parameters referable to intake of placebo.

Thus, we demonstrated a decline of physical work capacity during 6-h AOH, which is apparently related to redistribution of body fluids toward the upper part of the body and this is the cause of triggering mechanisms that alter a number of physiological functions [8].

It had been previously demonstrated that intake of sydnocarb during 7-day immersion of man maintains the parameters of oxygen uptake during maximum load on a bicycle ergometer, total volume of performed work and increases the amount of work per kg body weight [9].

We have demonstrated here that 3-fold intake of sydnocarb in a dosage of 25 mg during 6-h AOH has no appreciable effect on average MOU; however, work time and overall volume of work were greater with intake of sydnocarb than placebo.

With intake of DHE, the presence of some improvement of physical work capacity, as compared to intake of placebo, could be attributed to decreased deposition of blood in the veins of the lower limbs and increased venous influx to the heart.

Thus, with intake of the stimulating agent, sydnocarb, and DHE, which has a tonic effect on veins, during 6-h AOH, we observe a tendency toward some increase in physical work capacity judging by pedaling time on the bicycle ergometer and total volume of work. However, the principal criterion of work capacity, MOU, diminishes during 6-h AOH and remains low with intake of either sydnocarb or DHE.

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UDC: 613.693:92 Ivanov

OBITUARY OF DMITRIY IVANOVICH IVANOV

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 2, Mar-Apr 83 p 96

[Article by editorial board]

[Text] One of the veterans of Soviet aviation medicine, Dmitriy Ivanovich Ivanov, communist, colonel in the Medical Service retired, professor, doctor of medical sciences.

He was born in 1906 to a peasant family. In 1931, while studying at a medical institute, he joined the Party. In 1932, D. I. Ivanov was drafted in the Army, where he served up to 1969, and then worked as senior scientific associate. Dmitriy Ivanovich was bestowed the orders of the Red Banner, Red Star, "Honor Badge" and many medals.

For many years, the activities of D. I. Ivanov were related to high-altitude physiology, problems, the solutions of which were applied in practice. Dmitriy Ivanovich also made a perceptible contribution in the field of effects of inflight accelerations on the body, time reserve at different altitudes and prevention of altitude-caused complications.

Dmitriy Ivanovich was directly involved in implementing the first stratostat flights. He is one of the authors of many textbooks on aviation medicine.

The bright memory of Dmitriy Ivanovich Ivanov will remain in our hearts forever.

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